Control of ocular movement

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The ocular-motor system is organized to concentrate the images received by the eye upon the fovea, the most sensitive area of the retina. The acquisition and maintenance of object images upon the fovea, together with their stabilization during head movements, constitute the basic roles of human eye movement. These movements are simply motor outputs in response to sensory (primarily visual) inputs, but the precision of the system represents the most extraordinary example of sensory-motor integration carried out by the brain. This elegant system of fine movement, coupled with the accuracy with which eye position can be measured and the obvious (and potential) clinical correlation, accounts for the voluminous output of eye movement research in recent years. This deep interest is reflected in past (Bach-y-Rita, Collins and Hyde, 1971; Dichgans and Bizzi, 1972), present, and future symposia (a symposium entitled "Basic Mechanisms of Ocular Motility and Their Clinical Implications" is planned in Stockholm in June, 1974). The enormity of the subject boggles the mind of someone preparing a short talk.

I will not attempt an all-encompassing basic review of the subject but will concentrate upon:

- (1) Single unit recordings from the brain,
- (2) Extraocular muscle proprioception,
- (3) Some of our own investigations.

Single unit recordings

A major accomplishment in neurophysiology during the past decade has been the development of a technique for recording the activity from single nerve cells and fibres in the brains of alert monkeys who are behaving in their normal and usual fashion (Evarts, 1968). This method has been used to record from brainstem and cerebral structures while alert monkeys performed various eye movement tasks. The work from several laboratories are in general agreement (Fuchs and Luschei, 1970; Schiller, 1970; Robinson, 1970, 1972, 1973; Keller and Robinson, 1972; Luschei and Fuchs, 1972). The cells in the ocular-motor (oculo-motor, trochlear, and abducens) neuronal pools behave in a simple, stereotyped manner. During steady fixation, the discharge rate is quite constant and clearly related to the angle of gaze. As the eye is positioned progressively further in the direction of action of a particular muscle, the relevant neurones have proportionately higher firing rates. The discharge rate is dependent upon eye velocity as well as position. Robinson (1972) has expressed the discharge rate as a function of both position and velocity in a first order linear differential equation. The firing patterns of motor neurones can be predicted by this equation for every eye movement, *i.e.* saccades, pursuit, vergence, and vestibulo-ocular. Furthermore, contrary to previous speculations, all motor units seem to participate in all type of movement.

Henn and Cohen (1973), however, were unable to duplicate these firing patterns. They found that the firing frequency was related to *changes* in eye position, rather than to absolute position. This discrepancy may reflect methodological differences and will require further examination.

Analysis of single unit recordings from ocular motor neurones is obviously limited to sub-human primates, but very recent electronic developments suggest that analogous information can be obtained from a human ocular electromyogram (Trimble, Zuber, and Trimble, 1973).

Unit recordings from prenuclear structures in the brainstem have not yielded consistent results or enhanced our knowledge of supranuclear eye movement control except perhaps by attesting to its complexity. The situation with cortical recordings is of particular interest. Whereas neurones in the precentral motor cortex (Area 4 of Brodmann) discharge approximately 100 msec. before movement of the contralateral limb (Evarts, 1972), attempts at finding similar neurones which precede saccadic eye movements in the frontal eye fields have been unsuccessful (Bizzi, 1968; Bizzi and Schiller, 1970). Neurones were found which fired only *after* the eye movements. The implication is that saccades originate from sub-cortical structures; pre-onset neurones have been identified within the thalamus (Matsumami, 1972).

In the Bizzi studies, the cortical units were partially identified by antidromic responses to stimulation of the cerebral peduncle in the midbrain. Although there is a contribution of the so-called frontal eye fields to the peduncle, lesions of the latter do not produce any discernible eye movement abnormality. I question the wisdom of using peduncular stimulation to identify the cortical neurones but have no way of determining the degree of significance of this experimental flaw. Although I have been unable to find a single reported case of a saccadic palsy with a pathologically verified lesion *limited* to the contralateral frontal cortex, I continue to suspect that saccades originate in the frontal cortex.

The ocular motor system

Division of the ocular motor system into four separate sub-systems (saccadic, vergence, vestibular, and smooth pursuit) is of heuristic value and is distinctly helpful in the clinical examination:

(1) *Saccadic movements*

These occupy the exalted position of primacy! According to Jung (1972):

"Saccades determine the duration of fixations since all fixations are intersaccadic intervals. The (goal-directed saccade) *selects* the next target, *locates* it by foveal fixation, *terminates* the previous fixation period, and *cancels* (suppresses) its residual trace to avoid disturbance by multiple images of the visual world. *Thus saccades control the onset, duration and location of retinal images.*"

At the University of Maryland, considerable attention has been directed to the role of *microsaccades* which occur during fixation. These small saccades can be voluntarily inhibited and are not required to maintain target visibility by preventing retinal image stabilization (Steinman, Cunitz, Timberlake, and Herman, 1967). Microsaccades are used to scan the visual array in the same fashion as larger saccades (Haddad and Steinman, 1973).

(2) *Vergence movements*

These occur continuously. Most naturally occurring eye movements are compound,

consisting of both version (saccadic) and vergence components (Yarbus, 1967). The version and vergence sub-systems are functionally and anatomically independent, but their output sum algebraically to produce the compound movements. A short discussion of the retinal cues that evoke vergence movements was provided by Toates (1969). The vergence mechanism has been reviewed more recently by Zuber (1971), Westheimer (1971), and Jones and Kerr (1971).

True convergence paralysis, convergence insufficiency, and "A" pattern exotropia have been created by stereotactic midbrain lesions in man (Nashold and Seaber, 1972). These same patients also had paralysis of vertical gaze.

(3) *Vestibular movements*

Robinson (1972) reviewed recent information on the brainstem mechanisms involved in these movements. The vestibular mechanism provides the brainstem ocular motor system with information concerning changes in head position. However, the semi-circular canals are stimulated only by head acceleration. Thus, two integration steps are required to convert the acceleration signal into position information. The first step occurs within the end-organ itself and the second brainstem integration step is discussed and mapped out by Robinson (1972).

(4) *Smooth pursuit movements*

These are covered last because I will propose that these eye movements are not essential functions of the human organism (as are saccades, vergence, and vestibular movements). Rather, they represent a motor capacity which we utilize primarily in the unnatural settings of the clinical examination or research laboratory. My contention is based upon the following:

- (i) Smooth pursuit eye movements have never been experimentally created with cortical stimulation (admittedly no serious attempts to do this have yet been made).
- (ii) Patients who have grossly defective smooth pursuit eye movements ("saccadic" pursuit, such as seen with drug intoxication, Parkinsonism, cerebellar disease, etc.) do not complain that they are handicapped. Saccadic pursuit is a neuro-ophthalmological sign which produces no functional disturbance and no overt symptoms.
- (iii) In the afoveate rabbit, Collewyn (1971, 1972) and Collewyn and van der Mark (1972) demonstrated that the ocular motor system functions essentially as a retinal image-stabilizer. Optokinetic tracking, a highly artificial laboratory-induced task for the rabbit (analogous to smooth pursuit in the human), is accomplished by this stabilizing system. It is possible that humans and other primates also utilize a "fixation" mechanism to accomplish smooth pursuit, when so demanded. The relationship between fixation and smooth pursuit was certainly established by Yarbus (1967) who showed that humans can accurately pursue sinusoidal targets of ever-decreasing speeds which form a continuum with the omnipresent microdrifts of steady fixation.
- (iv) The primary requisites for the production of smooth pursuit are a co-operative subject, a moving target, and stabilization of the head. In our natural habitat of the real world, however, there are few objects which move in a slow predictable fashion and, more importantly, unless we have a stiff neck or are wearing a cervical collar, our heads are movable. Investigations of ramp and sinusoidal tracking in situations with freely moving heads indicate that the head rather than the eyes matches the target velocity and smooth

pursuit eye movements rarely occur (Fleming, Vossius, Bowman, and Johnson, 1969). Thus, except in unusual circumstances, humans do not utilize smooth pursuit eye movements; these movements should be regarded as laboratory “exercises”.

The above comments are not intended to disparage the importance of smooth pursuit eye movements for both the investigator and the clinician (Troost, Daroff, Weber, and Dell’Osso, 1972). For the former, the study of pursuit has yielded important information about the functioning of the nervous system, and I emphasize the necessity of examining both saccades and smooth pursuit eye movements in the neurological patient (Hoyt and Daroff, 1971).

There are occasional reports of subjects who can initiate and voluntarily control “pursuit” eye movements without a moving target (Heywood, 1972). Several investigators have utilized retinal after-images to generate similar “pursuit” or “smooth” movements (Steinbach and Pearce, 1972; Kommerell and Täumer, 1972). We prefer to restrict the term “smooth pursuit” to eye movements generated by a moving target; faulty theories may result from equating all slow versional eye movements with those of true pursuit.

As an outgrowth of the above, my associate Dr. Louis Dell’Osso has convinced me of the wisdom of another way of looking at the functional organization of the ocular motor system. The basic sub-divisions are Version and Vergence.

The various descriptions of eye movement outputs, in response to differing stimuli and experimental conditions, necessitate further division of the Version sub-system into two modes (*fast* and *slow*), both responding to a variety of inputs. The fast mode mediates all conjugate saccades, and the slow mode all conjugate slow movements. The latter includes, but is not limited to, the pursuit function. The slow mode also generates eye movements in response to volition, proprioceptive tracking of a moving hand in darkness (Steinbach, 1969), after-images, and vestibular input. This dual-mode (fast and slow) Version sub-system operates synergistically with the Vergence sub-system to comprise the total ocular motor control system responsible for the generation of all eye movements (Dell’Osso and Daroff, in press). The fast and slow modes of the Version sub-system originate separately in the cerebral hemispheres and first intermix anatomically at diencephalic and upper brainstem levels. Vestibular influences enter at the pontine level. The pontine paramedian reticular formation (PPRF), at the segmental level of the abducens nuclei, is the final prenuclear anatomical substrate for all horizontal versions, both fast and slow (Hoyt and Daroff, 1971). Convergence and vertical versions are controlled at midbrain levels (Nashold and Seaber, 1972).

Extraocular muscle proprioception

Before 1972, when I asked a medical student the questions “Is there conscious position sense from extraocular muscle?” or “Is there extraretinal position sense from the eyes?”, an affirmative answer was regarded as erroneous. I would, in a proper scholarly manner, expound somewhat as follows: The conscious position sense of the extremities is derived from joint receptors, structures which are not present in the orbit. There is no “muscle sense” in man; that is, extremity muscle stretch does not yield conscious position information (Gelfan and Carter, 1967). Furthermore, Brindley and Merton (1960) proved that the eye had no extraretinal position sense; subjects with anaesthetized conjunctiva were unable to detect passive movements of the globe in darkness.

At present, however, the proper answers to the cited questions would seem to be "yes". From Oxford came evidence that extremity muscle receptors can influence consciousness and indeed contribute to subjective awareness of limb position (Goodwin, McCloskey, and Matthews, 1972; Matthews, 1972). Moreover, Skavenski (1972) demonstrated conscious extraretinal position sense from the eyes in man which could be used to maintain eye position during displacement attempts in darkness. This experiment directly contradicts Brindley and Merton (1960) who, Skavenski argued, used coarse techniques which distracted the subjects from concentrating on the experimental task.

The historical reversals of thought have been remarkable. Helmholtz (1867) originally proposed an "outflow" (corollary discharge; efference copy) theory, contending that we know the position of our eyes in darkness only because we moved them there; knowledge of eye position derives from the command sent to the extraocular muscles. Sherrington (1918) later proposed that stretch receptors in extraocular muscles provided the conscious sense of position. Irvine and Ludvigh (1936) cast some doubt on the Sherrington notion which was finally "dispelled" by Brindley and Merton (1960). Skavenski (1972) swung the pendulum towards the Sherringtonians. However, the extraretinal inflow signal which can be used to control eye position, does not influence the perception of direction (Skavenski, Haddad, and Steinman, 1972); for this, "outflow" information is required.

The physiological role of the spindles in the precise control of eye movements is at present uncertain (Bach-y-Rita, 1971; Keller and Robinson, 1971; Stark, 1971) and many alternative possibilities have been expounded (Gurevich, 1960).

Personal investigations

I will conclude by describing some of our own studies. We organized an eye movement recording laboratory at the Miami Veterans Administration Hospital for the clinical study of patients with eye movement disorders. While recording normal subjects, to become familiar with the instrumentation, we were surprised to find that the termination of refixation saccades were not always conjugate. We discovered that most previous investigators studied only one eye or used bitemporal electrodes. This prompted a binocular electro-oculographic analysis of horizontal saccades in 25 normal human subjects (Weber and Daroff, 1971). We found that the major influence upon saccadic precision was the amplitude of the refixation. 70 per cent. of 10° saccades terminated conjugately and were normometric (required no correction). The remaining trials at this amplitude demonstrated conjugate undershoots (13 per cent.), overshoots (9 per cent.), or a brief disconjugacy (9.5 per cent.). At 20° , fewer saccades were normometric (43 per cent.), undershoots became more prevalent, overshoots decreased slightly, and disconjugacies increased. The tendency towards inaccuracy (dysmetria) was more evident at refixations of 30° . Here, fewer than 20 per cent. of trials were normometric, more than 50 per cent. undershot conjugately, overshoots were rare, and 27 per cent. terminated disconjugately. This last situation was usually produced by uniocular dysmetria—overshoot of the adducting eye or undershoot of the abducting eye. Combining saccades of all amplitudes, 46 per cent. (of 4,353 trials) were normometric, 37.5 per cent. were conjugately dysmetric (conjugate undershooting: 40 per cent.; conjugate overshooting: 6.5 per cent.), and 17 per cent. demonstrated disconjugate dysmetria (uniocular undershoot and/or overshoot.)

All the dysmetric saccades mentioned above were followed by a small corrective movement which accomplished alignment of the fovea with the new fixation target. We analysed these corrective movements and discussed possible feedback mechanisms involved in their

generation (Weber and Daroff, 1972). Conjugate dysmetria was corrected by a binocular high-velocity (saccadic) movement which began approximately 125 msec. after termination of the original refixation. Disconjugate errors were corrected by slow uniocular drift-like movements which were seemingly continuous with the termination of the original saccade. We designated these corrective movements as "glissadic" or "glissades". Saccadic corrective movements occurred in darkness which eliminated a possible role of visual feedback; but proprioceptive feedback was regarded as a possible explanation. Response feedback (proprioceptive or visual) could not explain the no-delay glissadic corrective movements, for which we proposed a prenuclear feedback mechanism that could monitor brainstem output, detect asymmetric outflow, and correct the situation "in flight".

Our concept of the "glissade" received some criticism but, we hope, survived (Dell'Osso, Daroff, and Troost, 1973). We presently suspect that these uniocular corrective movements may be mediated by the vergence sub-system in response to monitored disconjugate efferent output from the version sub-system.

We made a quantitative oculographic analysis of refixation saccades (Troost, Weber, and Daroff, 1972) and smooth pursuit eye movements (Troost, and others, 1972) in a 29-year-old man who had had a left cerebral hemispherectomy 11 years previously. Saccades in both directions were of equal velocity. Those to the right were grossly inaccurate and we established that this was not entirely due to the complete right homonymous defect. This study established the capability of each hemisphere to initiate saccades of equal and normal velocity in both directions. The patient could generate normal smooth pursuit to the right but leftward pursuit was always slower than the target velocity and required corrective saccades. The number of saccades was greatest at lower target speeds and decreased at higher speeds; the average amplitude of saccades increased monotonically with target velocity. Whereas the velocity gain (output/input) of his rightward pursuit approached unity, his leftward pursuit system exhibited a gain of approximately 0.24 to 0.34.

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Discussion

VON NOORDEN Regarding the theory that the type of eye movement is determined by the pattern of firing of the motor neurone, is there any correlation between the type of muscular fibre and the type of response which these fibres give?

DAROFF It is tempting to equate eye muscle characteristics with fast and slow eye movements; single cell brainstem recordings do not support such a correlation.

SANDERS Could you comment on why one does not see during pursuit movements, and on the saccadic system in relation to Dr. Ikeda's sensory findings of sustained or transient cells?

DAROFF The notion of complete loss of vision during a saccade is an exaggeration. Actually, the elevation of visual threshold is probably relatively small, being approximately 0.5 log units. The mechanism of this saccadic suppression is quite controversial, with some investigators favouring a central inhibitory process and others a peripheral effect related to retinal smear or shearing forces that develop between the vitreous and the retina. The cells which Dr. Ikeda described as commonly found in the periphery of the retina, *i.e.* "transient" cells, would be ideal for stimulating the nervous system to make a refixation saccade.

IKEDA There is another type (the third type) of retinal ganglion cell, known as “W” cells, found in the area centralis. This type could be suppressed by contrast and seemed to have very small receptive fields and axons terminating exclusively in the superior colliculus. So pursuit eye movements, tracking, or maintenance of fixation may be dependent on these “W” cells, although the saccadic mechanism may be dependent on “transient” neurones.

STRACHAN What is the function of the muscle spindles in the extraocular muscles?

DAROFF Many theories have been advanced concerning the role of the spindles but I do not regard any as being entirely satisfactory. Some investigators even claim that these spindles serve no useful function in the extraocular muscle but this hardly seems tenable.

GILKES Were you strictly correct in saying that the motor output responded to visual input?

DAROFF Motor output is primarily a response of the visual input, but other sensory inputs, such as those from the auditory and vestibular systems, contribute to the motor output.