SOME CONTRIBUTIONS TO THE STUDY OF SACCADIC EYE MOVEMENT CONTROL IN CAT, WITH AN EMPHASIS ON THE ROLE OF PREMOTOR CORTEX

by

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Résumé

La stimulation et l'enregistrement unitaire dans l'aire oculogyre frontale (AOF) du chat alerte ont été entrepris afin d'élucider le rôle de cette région corticale dans le contrôle des saccades oculaires. Des études complémentaires touchant l'influence d'une stimulation de l'AOF sur les réponses unitaires dans le collicule supérieur (CS), et les propriétés des mouvements oculaires rapides du chat, ont aussi été accomplies. Les résultats principaux sont: (1) L'AOF du chat est divisible en deux régions, dont une est l'homologue de l'AOF du singe tandis que l'autre semble impliquée dans la motricité de la tête. (2) Certaines cellules de l'AOF déchargent en bouffées avant ou après le début de la poursuite oculaire quand l'oeil se déplace dans une direction spécifique. (3) D'autres cellules déchargent en bouffées avant l'EMG des muscles du cou. (4) Les réponses visuelles d'unités dans le CS peuvent être modifiées suite à la stimulation de l'AOF. (5) Le déplacement de l'oeil en fonction du temps est le même pendant une saccade que pendant la phase rapide du nystagmus. (6) Les composantes horizontale et verticale d'une saccade oblique ne sont pas independantes sur le plan temporel.

ABSTRACT

The results of stimulating and recording in the frontal eye field (FEF) of alert cats are described with the aim of elucidating the role of this cortical area in the control of saccadic eye movements. Complementary studies are presented of the influences of FEF stimulation on unit responses in the superior colliculus (SC); and of some basic properties of cat rapid eye movements. The main findings are: (1) a subdivision of the cat FEF into two areas, one of which seems homologous to the monkey FEF, while the other seems related to head movement control; (2) FEF units whose discharges are related to ocular tracking in specific directions; (3) FEF units whose discharges precede neck muscle activity; (4) units in the SC whose visual responses are modified by FEF stimulation; (5) identical temporal properties of saccades and the quick phases of vestibular nystagmus; and (6) temporal dependence between the orthogonal components of oblique saccades.

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This thesis represents the results of an adventure I hesitatingly embarked upon some years ago after receiving a Ph.D. in mechanical engineering. As I write these lines some old and familiar faces reappear before me: some encouraging me to try the adventure, others discouraging me; others noncommittal.

John O'Keefe of University College, London, England, probably bears the greatest responsibility for my having converted to the biological sciences.

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PREFACE

The Faculty of Graduate Studies and Research of McGill University in their bulletin, Guidelines Concerning Thesis Preparation, section 7 (cited in full below*) permits the submission of a thesis consisting of a collection of original papers. This work is organized in accordance with this option. Chapters which have either been submitted for publication, are in press, or have been published are so identified.

Chapter 1 serves as an introduction to the overall work. In it the organization of the thesis is explained and an overview of the contents is given. In accordance with the format each chapter includes a discussion, references, figures and conclusions appropriate to the material presented therein. To complement this, a brief section is included at the end to summarize, conclude and indicate clearly the contributions of this thesis to original knowledge.

It should be noted that the format for the references varies from chapter to chapter and is based on the requirements of the journal to which the article has been submitted, or in which it has been published. Furthermore, references cited in the text, referring to previous articles by the author which are contained in this thesis, are made to the original publication. The following equivalence should therefore be borne in mind.

Reference	Full Reference	Chapter in Thesis
Ferch and Guitton in preparation	A system for recording eye movements using phase locked loop demodulation of an electro-magnetically induced eye coil signal. (to be submitted to Vision Research)	Chapter 2
Guitton and Mandl (1974)	The effect of frontal eye field stimulation on unit activity in the superior colliculus of the cat. Brain Research 68 (1974) 330-334	Chapter 8

Reference	Full Reference	Chapter in Thesis
Guitton and Mandl (1976)	The convergence of inputs from the retina and the frontal eye fields upon the superior colliculus of the cat. Expl. Brain Res. Suppl.1 (1976) 556-562.	Chapter 8
Guitton and Mandl (1978a)	Frontal 'oculomotor' area in alert cat. I. Eye movements and neck activity evoked by stimulation. Brain Res. 149 (1978) 295-312.	Chapter 6
Guitton and Mandl (1978b)	Frontal 'oculomotor' area in alert cat. II. Unit discharges associated with eye movements and neck muscle activity. Brain Res. 149 (1978) 313-327.	Chapter 7

*Section 7 of 'Guidelines concerning thesis preparation', McGill University, Faculty of Graduate Studies and Research.

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TABLE OF CONTENTS

PAGE

SECTION 2

PAGE

SECTION 3

Cortical Control of Eye Movements: The Role of the Frontal Eye Field

PAGE

SECTION 3

PAGE

SECTION 5

SECTION 1

INTRODUCTION, THESIS ORGANIZATION, OVERVIEW OF CONTENTS, AND SOME SPECIAL ASPECTS OF THE METHODOLOGY

CHAPTER 1

INTRODUCTION, THESIS ORGANIZATION, AND OVERVIEW OF CONTENTS

INTRODUCTION, THESIS ORGANIZATION, AND OVERVIEW OF CONTENTS

Compared to the rich repertoire of possible spatio-temporal trajectories associated with limb movements, the manner in which we move our eyes appears quite restricted. Indeed, voluntary eye movements have stereotyped time courses and cannot be generated with either an arbitrarily willed velocity or trajectory. The gaze axis can be displaced from one point of interest to another only by using the rapid, almost discontinuous movements called saccades. Furthermore, under most normal circumstances slow eye movements can only be made when moving targets are tracked, and the ability to pursue smoothly saturates at fairly low velocities (about 40^{o}/sec; Young, 1971). For these and other reasons the neural systems that control ocular motility are thought to be simpler than those that control limb movement.

In recent years there has been much progress in our understanding of the basic neural mechanisms responsible for controlling ocular movements. Detailed studies have now been made of the various force patterns required either to hold the eye fixed in an eccentric position, or to generate smooth pursuit or saccadic movements (Robinson, 1964; Robinson, 1965; Collins, 1975; Collins, O'Meara and Scott, 1975). Complementary studies have considered the neural signals innervating the extra-ocular muscles during these eye movements (Collins, 1975). In addition, the discharge characteristics of motoneurons have been extensively recorded in the extra-ocular motor nuclei of alert behaving monkeys (Fuchs and Luschei, 1970; Robinson, 1970; Robinson and Keller, 1972; Henn and Cohen, 1973). Contemporary research is now focussing primarily on the immediate supra-

nuclear mechanisms responsible for the generation of eye movements (see Keller, 1977, for review).

Nearly all our knowledge about the functional properties of neurons implicated in oculomotor control has come from single unit recording in the alert monkey. It is no surprise, however, that a great deal of morphological and electrophysiological information has at the same time been gathered about the oculomotor circuitry of the domestic cat, a species widely utilized as a laboratory acute preparation. Important questions arise: are the results of one species applicable to the other? If not, what can we learn from differences?

One difference between cat and monkey that is becoming increasingly evident relates to the control of eye-head coordination. This is suggested by the different patterns of eye and head movements evoked by micro-stimulation of the superior colliculus at positions corresponding to different retinal eccentricities (Crommelinck, Guitton and Roucoux, 1977a; Guitton, Roucoux and Crommelinck, 1977). The cat's oculomotor range is limited to about $\pm$ 23° from the central gaze position (Crommelinck, Guitton and Roucoux, 1977b). The retina has receptive fields that extend at least to 55° from the area centralis (Enroth-Cugell and Robson, 1966). Thus, unlike monkey, visual stimuli impinging on the cat retina at angular distances greater than 23° cannot be acquired using simply an eye movement.

When the research described in this thesis was begun, very little was known about eye movements in cat. Indeed, frequently it had been suggested that cats rarely seemed to move their eyes at all, and that changes in gaze position seemed predominantly accomplished by movements of the head. In the only study of cat saccades, available at that time (Stryker and Blakemore, 1972), the eye movements were measured by videotape display and

electro-oculography, and the results showed that unlike for man and monkey, there existed a poor correlation between saccadic velocity and amplitude.

One particular aim of this thesis was to provide more information about rapid eye movements in cat. This knowledge was important to realize the general aim of the overall research program, which was to provide greater insight into cortical and cortico - brainstem influences on oculomotor control. In this program it was intended, in part, to record unit discharges in the frontal cortex of alert cats while they performed various eye movement manoeuvres. The appropriate planning of these experiments, and analysis of their results, would require that sufficient knowledge be available on the oculomotor behaviour of the normal cat. The experiments on ocular movements also aimed at providing a "test-bed" for the novel eye movement recording system that was developed during the course of this research (see below). The development of this system constituted, in a sense, another aim of the present research program which was to establish the basis for a long-term study of visuo-motor mechanisms.

The research on eye movements is described in Chapters 3 and 4. The quantities, amplitude, duration, and maximum velocity that characterize rapid eye movements were first obtained for saccades made in the light. These were then compared to the more reflexive rapid movements called the quick phases of vestibular nystagmus. It was also of interest to determine whether cats could make voluntary eye movements in the dark, and if so, how these movements compared to saccades made in the light. Horizontal and vertical saccades were also compared and a study was made of how these orthogonal movements combine to form oblique saccades.

Although brainstem mechanisms implicated in oculomotor control have been intensively studied, there is very little known about the associated cortical mechanisms and their influence on the immediate supranuclear neural circuits. Two functions have been extensively discussed in relation to the role of the cortex in oculomotor behaviour.

The first regards the neural command center controlling voluntary eye movements. This function has classically been attributed to the frontal eye field (FEF, area 8). The FEF, by virtue of its strong projection unto the superior colliculus (SC) of monkey (Astruc, 1971; Künzle, Akert and Wurtz, 1976; Künzle and Akert, 1977), has been thought to mediate voluntary control over brainstem controlled reflexive orienting movements (Holmes, 1938).

The second is the intriguing and almost philosophical question (MacKay,1972) regarding the brain's ability to distinguish between those peripheral sensory inputs that are due to self movement, and those that are caused by independent action within the external world. In visual perception this mechanism implies that afferent information from the retina is analyzed in conjunction with information from the oculomotor system. Normally, the perception of movement in visual space is thought to originate with motion of an image on the retina, reflecting a "real" movement in the visual field. However, there is no such perception of movement when identical retinal image motion is caused by the eye sweeping over a stationary background. It has long been assumed that an extra-retinal signal (internal motor feedback, efference copy or corollary discharge) might be responsible for the modification of unit responses in a sensory structure during eye movements (Sperry, 1950; Holst, 1953). It has been

suggested that the frontal lobe might mediate this corollary discharge (Teuber, 1960) and that the SC may be a relevant target.

It is interesting that the FEF and SC have been implicated in both the voluntary control of eye movements and in the corollary discharge mechanism. Neurons in the SC are highly sensitive to moving patterns presented before the immobile eye (Sterling and Wickelgren, 1969; Mandl, 1974). Consequently, in addition to its classically suggested role as a structure controlling the ability to orient towards a peripheral visual stimulus (Schiller and Koerner, 1971; Schiller, 1972; Schiller and Stryker, 1972; Wurtz and Goldberg, 1972; Wurtz and Mohler, 1976; Sparks and Pollack, 1977), the SC has also been thought to play a role in the visual perception of movement (Anderson and Symmes, 1969; Mandl, 1974).

If the role of the FEF in monkey is poorly understood, then its function in cat is even more of an enigma. One aim of this thesis was to provide more information on the functional role of the FEF in cat, and to investigate its link with the SC. The early stages of the experimental program were devoted to a study of the influence of the FEF on the SC. The frontal lobe of cat was electrically stimulated at sites where previous experiments had shown that eye movements could be evoked (Schlag and Schlag-Rey, 1970). The effect of this stimulation on unit activity of single cells in the SC was observed and it was found that FEF stimulation could modify the visual responses of some collicular cells, as well as excite other non-visual ones. This work is described in Chapter 8.

The interpretation of these early results was limited by the scant knowledge available on the frontal oculomotor region of cat. It was known that eye movements could be elicited from a reasonably well established

region of frontal cortex (Hassler, 1966; Schlag and Schlag-Rey, 1970) and that ablation of this zone caused, like in monkey, perserverative tracking and fixation (Jeannerod, Kiyono and Mouret, 1968). But the characteristics of eye movements (direction, latency, and amplitude) evoked by stimulation were either not available, or were not agreed upon, and no unit activity had previously been monitored. The existence of a homology between cat frontal oculomotor area and monkey FEF was therefore quite uncertain. Before attempting to describe frontal lobe - SC interaction in more detail, it was therefore decided to embark on a program of research whose general objective was to clarify the role of the frontal oculomotor region in cat, and whose particular aim was to offer data useful in determining whether or not a functional homology existed between the frontal oculomotor region of cat and the FEF of monkey. Experiments involving stimulation and recording were therefore begun in cat (chapters 6 and 7).

In the experiments to be described, the discharge characteristics of single units in the frontal oculomotor region of cat were monitored and compared while alert but naive animals: (1) made spontaneous eye movements in either the light or the dark; (2) attentively tracked targets moving either "randomly" or periodically; and (3) were rotated in the horizontal plane in both the light and the dark to induce vestibular nystagmus.

It is known that FEF lesions are frequently associated with the initial inability to move the eyes; the tendency to persevere in tracking a target; and a deficiency in unpractised visual search. The rationale for using naive animals performing tasks 1 and 2, described above, was that the study of single cell discharges could be made while cats exhibited behaviour known to be affected by FEF ablation. As the FEF is also thought to be involved in the control of head movements (Bizzi and Schiller, 1970),

it was decided to pay particular attention to the relation between unit discharges and neck muscle activity. The work describing unit response characteristics is described in Chapter 7.

In view of a possible oculomotor command function ascribed to the FEF, a study was also undertaken of the effects of stimulating the cat frontal oculomotor area. This work is described in Chapter 6. The results were compared with those already available for monkey, to yield further clues on the possible homology between frontal eye fields of the two species. The stimulation and unit studies were linked by a technique that has previously been used in the cat motor cortex (Asanuma, Stoney and Abzug, 1968). Threshold focal stimulation was applied at those sites where units had just previously been recorded. In this way the direction and amplitude of eye movements and their associated neck muscle EMG activity, evoked by stimulating a given point in the cortex, could be compared directly with similar saccades and EMG generated spontaneously by the animal in association with unit discharges recorded at that point. This information, in conjunction with knowledge of the threshold current necessary for evoking eye and head movements should, for example, be useful in elucidating the possible role of the FEF in coordinated eye and head movement control.

The experimental program has necessitated the development of techniques relevant to the recording of eye movements in alert cat preparations. Many techniques have been developed for doing this and a recent concise review has been given by Collewijn, Van der Mark and Jansen (1975). The technique which is at present most valued in laboratory experiments involving animals was originally designed by Robinson (1963) for use in human experiments and was later developed by Fuchs and Robinson (1966) for use in monkeys. In animal preparations the method requires that a coil of

fine wire be implanted around the eyeball beneath the recti muscles and the bulbar conjunctiva. When the eye rotates the plane of the implanted coil rotates through an equal angle. The animal's head is placed in two orthogonal AC magnetic fields which in Robinson's original apparatus were in phase quadrature. The magnetic fields induce a current in the eye coil which is related to the angle of the eye with respect to each magnetic field. A phase detection system then analyses the voltage across the eye coil and separates the effects due to each of the two fields. Two output signals result, each being proportional to the sine of the angle that the eye makes with respect to the horizontal and vertical planes, respectively.

The significant advantages of the eye coil method are:

(1) The calibration of the eye coil is very stable. Any drift which may occur during a recording session is due to the electronics and, though small, can be readily assessed by calibrating with a dummy search coil at regular intervals.

(2) The system does not require eye movements by the subject, in order to obtain a calibration. Instead, the field coil surrounding the subject can be moved whenever the eye is stationary. This capability is useful when using the system with cats not trained to make eye movements to specific points in their visual field.

(3) The system is more sensitive than most other methods (< 15 min. arc).

(4) The visual field is not obstructed (cf. systems using infrared reflection, or video/film recording).

(5) The calibration, unlike in EOG, is the same in both light and dark. Furthermore, the output is insensitive to closure of the eyelids and electro-myographic interference.

The eye-coil technique was judged ideal for the present experimental program. However, the system as originally described by Robinson (1963) used phase coding and was found to be expensive. Also, the low frequency used to operate the field coils suggested probable noise interference with unit recordings. Consequently a new approach using frequency coding, was devised. This is described in Chapter 2.

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CHAPTER 2

A SYSTEM FOR RECORDING EYE MOVEMENTS USING PHASE LOCKED LOOP DEMODULATION OF AN ELECTRO-MAGNETICALLY INDUCED EYE COIL SIGNAL

Status: Submitted to Vision Research

ABSTRACT

A system is described which permits the accurate measurement of horizontal and vertical eye movements using the voltage induced in a coil of wire attached to the eye and placedin two orthogonal, spatially fixed and alternating magnetic fields. The system uses frequency rather than phase coding, with the pairs of field coils operating at different frequencies (60 KHz and 120 KHz respectively). The mixed signal induced in the eye coil is decoded by separating the frequencies using an integrated circuit Phase Locked Loop. The system is inexpensive to build and can detect eye movements smaller than 10 min arc.

A SYSTEM FOR RECORDING EYE MOVEMENTS

INTRODUCTION

An excellent method for precisely recording eye movements has been described by Robinson (1963). The technique consists of attaching to the eye a coil of fine wire which is then subjected to two orthogonal, spatially fixed but alternating magnetic fields. According to Faraday's law, a voltage is induced in the coil and this signal is a function of the orientation of the gaze axis with respect to each magnetic field. The measurement of eye movements in humans can be made with the coil of wire imbedded in a contact lens (Robinson, 1963) or an annular ring (Collewijn et al., 1975), attached by suction to the eye. In animal experiments the coil of fine wire is usually implanted around the eyeball, under the bulbar conjunctiva and beneath the insertions of the recti muscles (Fuchs and Robinson, 1966).

The advantages of the eye coil system over other techniques have been described elsewhere (Collewijn et al., 1975). Some of these advantages are its stability and insensitivity to surrounding illumination, closure of the eyelids, and translational movements of the head. The system can be calibrated by simply rotating the field coils, with eyes stationary. This useful characteristic eliminates the need to calibrate by having the animal fixate specific points in its visual field.

The horizontal and vertical components of each eye movement can be deduced using different methods. In the one originally described by Robinson (1963) the two magnetic fields are in phase quadrature and their respective contributions to the eye coil signal are obtained using a phase detection system. Another possibility is to generate magnetic fields having different frequencies. This is the basis of the system to be described in the present paper. Another system has recently been designed (McElligott, Loughname and Mays, 1979) that uses the present circuit for generating the magnetic fields, but a different technique for demodulating the eye coil signal.

Principles of Operation

(Fig. 1 near here)

A coordinate system is defined (Fig. 1) such that the y axis corresponds to the primary gaze position and the z and x axes are vertical and horizontal, respectively. The angles α and β specify the instantaneous gaze directions given by vector $\overline{G}$. The plane of the eye coil is normal to $\overline{G}$. According to Faraday's law, the electromotive force (emf) in a coil is given by

$$e = N \frac{d\Phi}{dt} \qquad (1)$$

where e is the emf in volts, N is the number of turns in the coil, and t is the time in seconds. Φ is the magnetic flux, in webers, and is defined by

$$\Phi = \int \overline{B} \cdot d\overline{A} \qquad (2)$$

where vector $\overline{B}$ is the magnetic flux density in webers/m^2 and $\overline{A}$ is the vector area of the coil in m^2. The vector area can also be written

$$\overline{A} = A\,\overline{n} \qquad (3)$$

where $\overline{n}$ is the unit vector normal to the coil surface and which lies along $\overline{G}$. A is the coil area.

Thus

$$\Phi = \int \overline{B} \cdot \overline{n}\, dA \qquad (4)$$

The coils that generate the magnetic fields are designed such that the fields are uniform in the vicinity of the eye coil (Robinson, 1963). Therefore

$$\Phi = A \bar{B} \cdot \bar{n} \qquad (5)$$

In the region of the eye coil the magnetic fields are directed along the $\underline{z}$ and $\underline{x}$ axes and therefore

$$\bar{B} = B_x \bar{i} + B_z \bar{k} \qquad (6)$$

The unit vector $\underline{\bar{n}}$ is given by

$$\bar{n} = \cos \alpha \sin \beta \bar{i} + \cos \alpha \cos \beta \bar{j} + \sin \alpha \bar{k} \qquad (7)$$

where $\underline{\bar{i}}$, $\underline{\bar{j}}$ and $\underline{\bar{k}}$ are the unit orthogonal vectors. Performing the vector multiplication yields

$$\Phi = A (B_x \cos \alpha \sin \beta + B_z \sin \alpha) \qquad (8)$$

Let the vertical and horizontal magnetic fields be modulated at frequencies ω_z and ω_x respectively

$$\begin{aligned} B_x &= B_{ox} \sin \omega_x t \\ B_z &= B_{oz} \sin \omega_z t \end{aligned} \qquad (9)$$

where B_{ox} and B_{oz} are the amplitudes in the vicinity of the eye coil. Substituting equations (8) and (9) in (1) yields

$$\begin{aligned} e = AN (&\omega_x B_{ox} \cos \alpha \sin \beta \cos \omega_x t + \omega_z B_{oz} \sin \alpha \cos \omega_z t \\ &+ B_{ox} \cos \alpha \cos \beta \sin \omega_x t \frac{d\beta}{dt} - B_{ox} \sin \alpha \sin \beta \sin \omega_x t \frac{d\alpha}{dt} \\ &+ B_{oz} \cos \alpha \sin \omega_z t \frac{d\alpha}{dt}) \end{aligned} \qquad (10)$$

The first two terms in this equation account for that part of the voltage in the eye coil due to the time varying magnetic fields. The last three terms account for motion of the eye coil within the field. To facilitate usage of the system, it is of interest that a calibration obtained with an immobile eye be applicable even when the eye moves. For this to be true

$$\frac{1}{\omega_z} \frac{d\alpha}{dt} << 1$$

and (11)

$$\frac{1}{\omega_x} \frac{d\beta}{dt} << 1$$

A lower limit on the operating frequency of the system may be calculated from equations (11) if the velocity of the fastest eye movement that is likely to be measured is known. This corresponds to a monkey's 30^o saccade where the maximum velocity is about 950^o (see Fuchs, 1967). Substituting this value into either of equations (11) yields:

$$f >> 2.6 \text{ Hz} \qquad (12)$$

where f is the modulation frequency in Hertz. This criterion will be largely met in the present system and it is possible to consider only the case where the eye is immobile: i.e. $\frac{d\alpha}{dt} = \frac{d\beta}{dt} = 0$. By appropriate filtering, the signal $\underline{e}$ can be split into two signals of frequencies ω_x and ω_z

$$e_\alpha = AN \omega_z B_{oz} \cos \omega_z t \sin \alpha \qquad (13 \quad (13)$$

$$e_\beta = AN \omega_x B_{ox} \cos \omega_x t \cos \alpha \sin \beta \qquad (14)$$

when $\omega_x = \omega_z$ these relations are similar to equations derived by Robinson (1963).

If α and β are less than 20° the following relations hold within 2% :

$$e_{\alpha} = (AN\ \omega_z\ B_{oz} \cos \omega_z t)\ \alpha \qquad (15)$$

$$e_{\beta} = (AN\ \omega_x\ B_{ox} \cos \omega_x t)\ \beta \qquad (16)$$

When either α or β change from a positive to an equal but negative value there is a sign change equivalent to a 180° phase shift, but the amplitude of the signal remains unchanged. The present system's operation is based on amplitude modulation, and to detect both positive or negative angles, it is necessary to insert a fixed bias coil in series with the eye coil. This bias coil also intercepts both the magnetic fields. The signals across both coils, after filtering, are

$$e_{\alpha} = AN\ \omega_z\ B_{oz}\ (\alpha + k_{\alpha}\ \alpha_B) \cos \omega_z t \qquad (17)$$

$$e_{\beta} = AN\ \omega_x\ B_{ox}\ (\beta + k_{\beta}\ \beta_B) \cos \omega_x t \qquad (18)$$

Subscript B denotes the bias coil. The constants k_{α} and k_{β} account for differences between the eye coil and the bias coil with respect to their area, number of turns, and position within the fields. The bias coil is adjusted such that

$$k_{\alpha}\ \alpha_B > \alpha_{MIN}$$

$$k_{\beta}\ \beta_B > \beta_{MIN}$$

where α_{MIN} and β_{MIN} represent the largest negative gaze directions to be measured. With this setting of the bias coil it is possible to vary α and β over their complete range and still maintain positive amplitudes in equations (17) and (18).

Figs. 2 and 3 near here

Description of the system

Operation of the system requires the design of two separate electronic circuits: one for generating both the horizontal and vertical magnetic fields; and the other for demodulating the signal induced in the coil of wire that has been wound about the animal's eye. Fig. 2 shows a block diagram of the system, while Figs. 3 and 4 show the detailed circuitry.

Field Generation (see Figs. 2A and 3)

The system was designed for field coils of approximately 50 cm in diameter. These were about 30 and 15 turns of copper wire(20 AWG Hvy armored ply thermalize) in each of the pair of coils comprising the 60 and 120 KHz systems, respectively. The field coils were arranged in a box shaped structure (a cube), 50 cm on edge. It is important that the field coils be designed to minimize electrostatic coupling with the eye and bias coils. Initially, aluminum foil was wrapped about each field coil, as described by Robinson (1963), but at the frequencies used here this technique proved to be unsatisfactory. Successful shielding can be obtained by using aluminum channel shaped to a circle, but interrupted by an insulating gap to avoid a short-circuited turn. The field coils are wound within the "U" of the channel and each channel is carefully grounded.

In the present system, the operating frequencies are chosen to be 60 KHz and 120 KHz, thereby reducing interference with physiological recordings.

The magnetic fields are generated by a free running 240 KHz oscillator. The oscillator output is a pulse train and the pulses are converted to square waves of two different frequencies by using two "divide-by-two" circuits. These square waves are passively filtered to provide sinusoidal

drive into each pair of low Q tuned field coils. Tuning is obtained by selecting the capacitance in parallel with the field coils (Fig. 3) so as to obtain maximum signal on a search coil (dummy eye coil) placed at the centre of the structure. Note that the number of turns of wire in the field coils in combination with the electrostatic shielding yields the low value of Q. This in turn assures that small drifts in frequency do not significantly affect the field strength.

Demodulator Channels (see Figs. 2B and 4)

Each demodulator channel is essentially an AM receiver operating at a specific frequency. Details on the construction of such an AM receiver, including a buffer stage which compensates for power supply variations and PLL thermal drift, are given by Signetics Corp., (1972). Only a brief summary is given here.

Accurate demodulation of the mixed signal induced in both the eye and bias coils is obtained by using a Signetics NE 561B Phase Locked Loop (PLL, Signetics Corp., 1972). This integrated circuit contains a voltage controlled oscillator (VCO) whose frequency can be made to lock to a specific input frequency: in this case 120 KHz for the PLL in channel 1 and 60 KHz for the PLL in channel 2. The locking frequency is obtained by adjusting C_o and C_y to the values given in the legend of Fig. 4. The output of the VCO has no amplitude modulation but the 561B PLL contains a multiplier (or product detector) which retrieves the variations in amplitude of the input signal resulting from movements of the eye coil. A simple passive filter precedes each PLL to facilitate capture, by the VCO, of the appropriate channel frequency. The output of the PLL contains a significant DC component (about 10V) which is reduced to a convenient lower value by the output buffer stage.

System Characteristics

With a search coil of 3 turns wound about a cat's eye (average diameter about 2.2 cm), the amplitude of the induced sinusoidal signal was about 7 μv/deg within the linear part of the response (± 20°). At the PLL output the DC signal sensitivity was 8 mv/deg, and the noise level 1 mv peak-to-peak. This permitted detection of eye movements as small as 1/8° in amplitude.

The response of the system to a sudden change in the amplitude of the input signal, such as is produced by a step displacement of the eye (a saccade does nearly this) is dependent on the characteristics of the filter at the output of the PLL. This filter is necessary to attenuate the high frequency harmonics (principally 120 KHz and 240 KHz) which are produced by the product detector. It follows that some tradeoff between frequency response and residual output ripple seems inevitable. The present system had a low pass frequency response characteristic having a corner frequency of about 1000 Hz.

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Fig. 1 (Fig. 2-1)

Coordinate system used for describing eye movements. Planes xy and yz are horizontal and vertical respectively. The y axis corresponds to the primary (or central) gaze position. Vector $\overline{G}$ denotes instantaneous gaze direction. Angles α and β measure vertical and horizontal gaze, respectively.

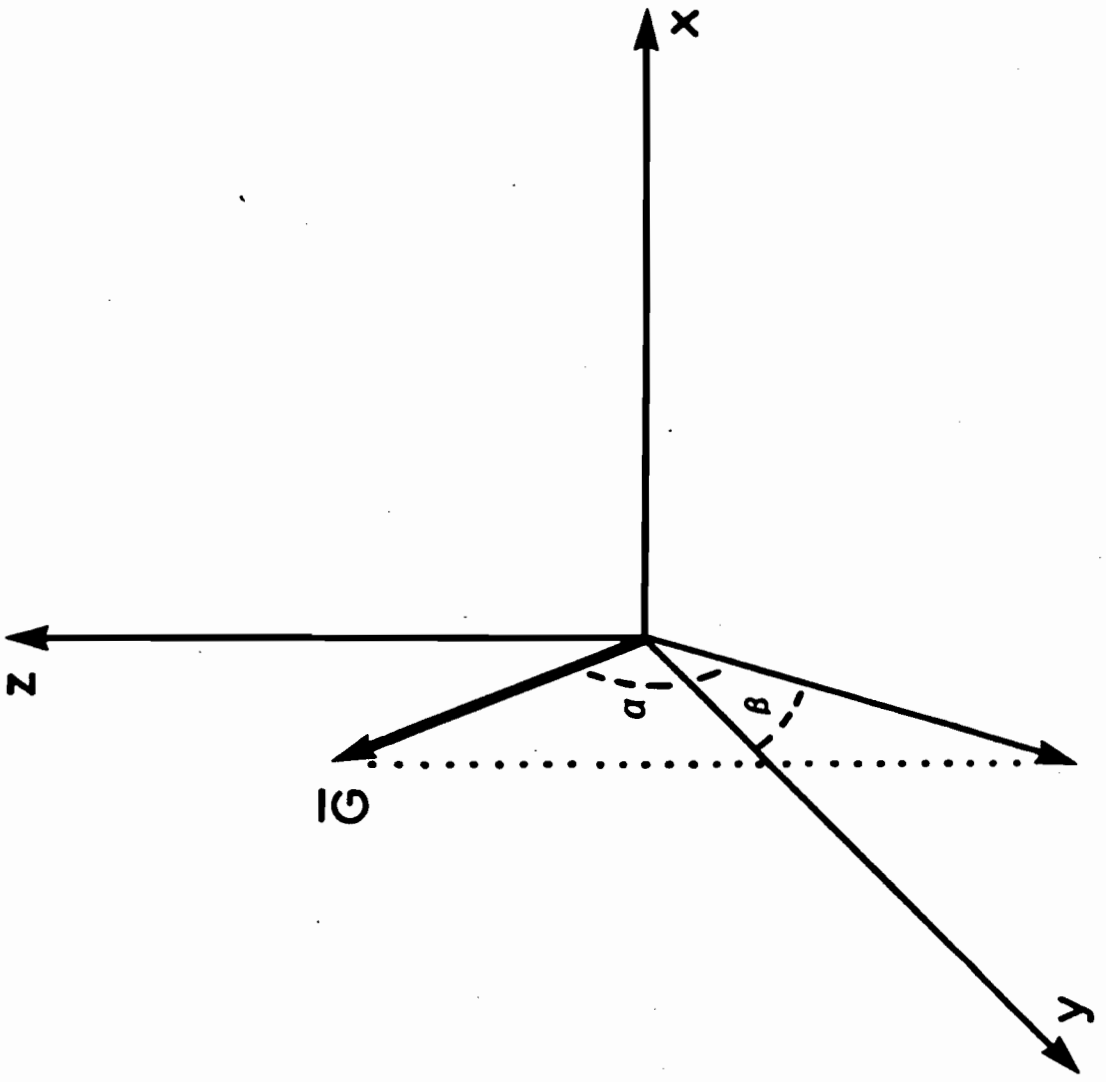
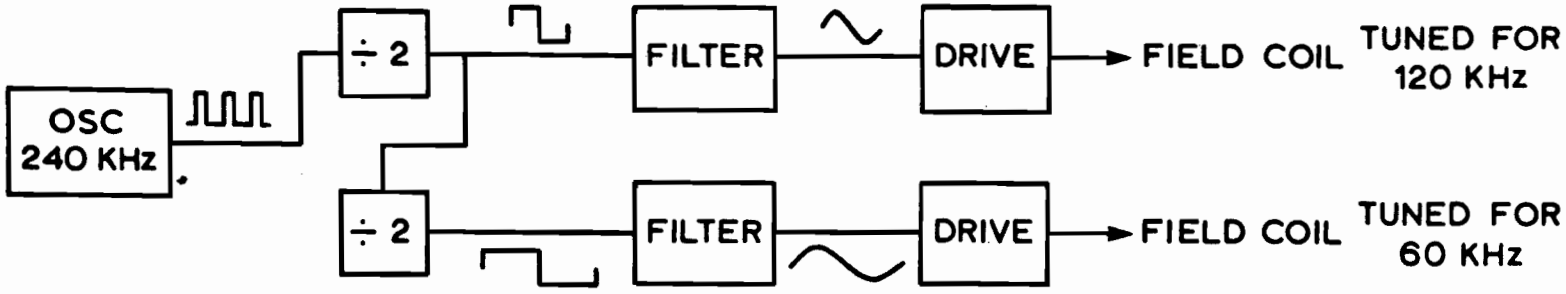

X
Z
IG
α
β
Y

Fig. 2 (Fig. 2-2)

Block diagrams. A. System for driving a pair of orthogonal field coils at two different frequencies. B. Demodulator channels which decode mixed frequency signal induced in eye and bias coils. The demodulator outputs correspond to horizontal and vertical eye positions, respectively.

A


OSC
240 KHz
÷ 2
FILTER
DRIVE
FIELD COIL
TUNED FOR
120 KHz
÷ 2
FILTER
DRIVE
FIELD COIL
TUNED FOR
60 KHz

B

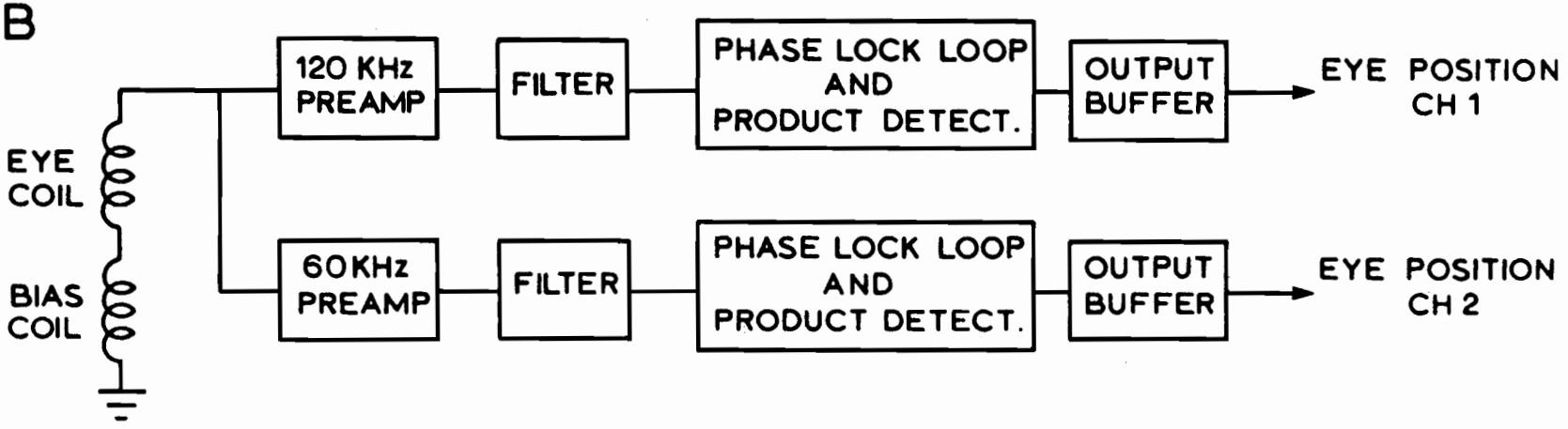

EYE
COIL
BIAS
COIL
120 KHz
PREAMP
FILTER
PHASE LOCK LOOP
AND
PRODUCT DETECT.
OUTPUT
BUFFER
EYE POSITION
CH 1
60KHz
PREAMP
FILTER
PHASE LOCK LOOP
AND
PRODUCT DETECT.
OUTPUT
BUFFER
EYE POSITION
CH 2

Fig. 3 (Fig. 2-3)

Circuit diagram of the system used to drive the pair of orthogonal field coils at two different frequencies. (See block diagram in Fig. 2A).

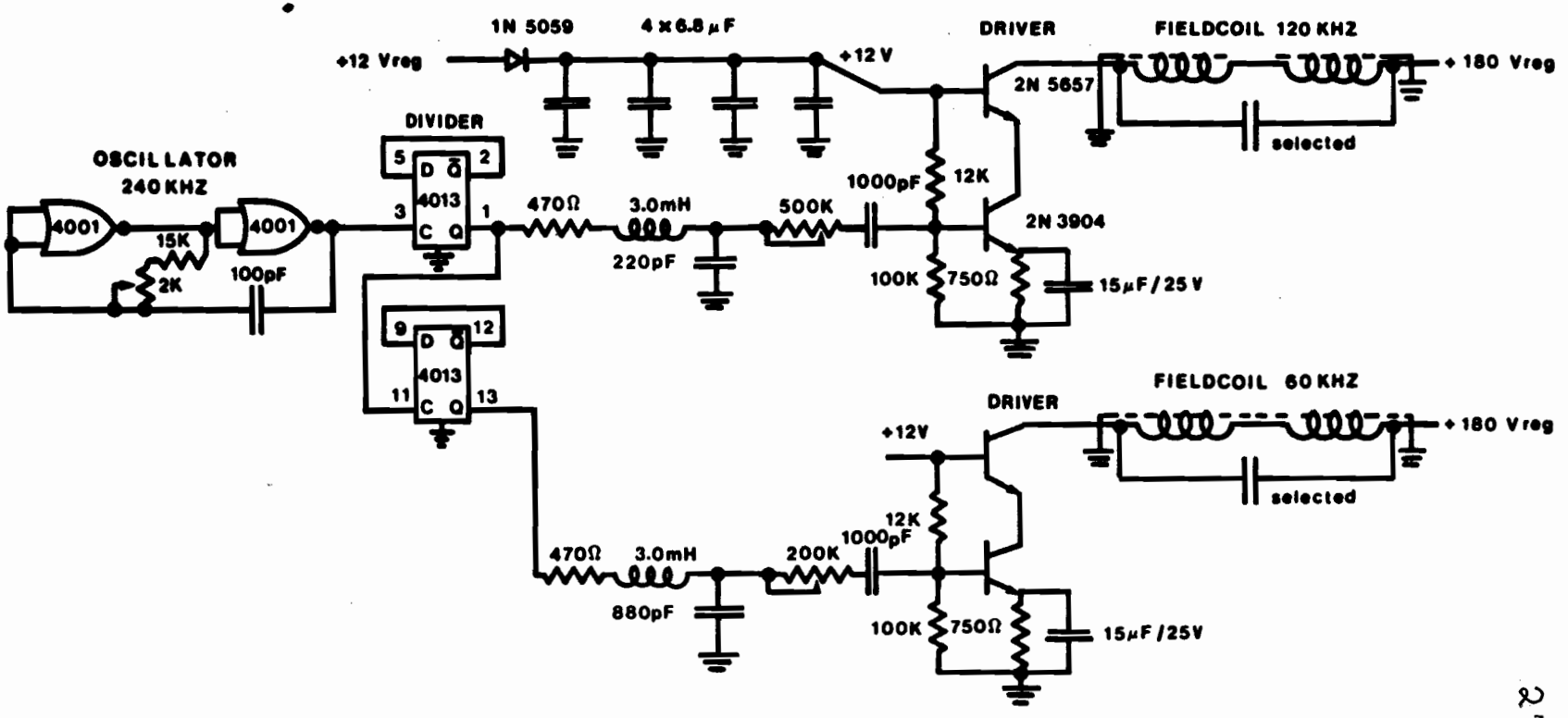
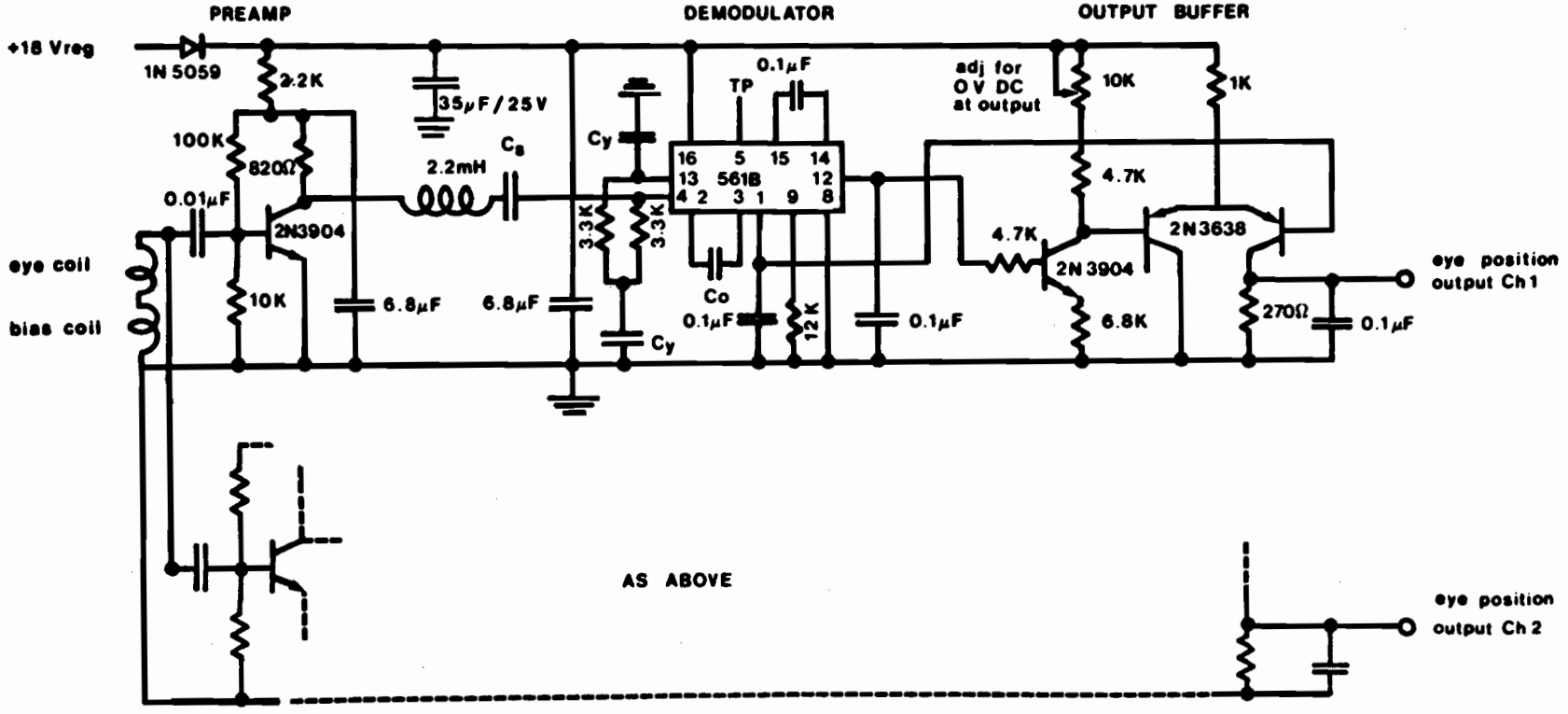

1N 5059
4 x 6.8 µF
+12 Vreg
+12 V
DRIVER
FIELDCOIL 120 KHZ
2N 5657
+ 180 Vreg
selected
DIVIDER
OSCILLATOR
240 KHZ
4001
4001
15K
2K
100pF
5
D
Q
2
4013
C
Q
3
1
470Ω
3.0mH
220pF
500K
1000pF
12K
2N 3904
100K
750Ω
15µF/25 V
9
12
11
13
FIELDCOIL 60 KHZ
DRIVER
+12V
+ 180 Vreg
selected
12K
1000pF
470Ω
3.0mH
200K
880pF
100K
750Ω
15µF/25V

Fig. 4 (Fig. 2-4)

Circuit diagram of the demodulation channels which decode the mixed frequency signal induced in the eye and bias coils. (See block diagram in Fig. 2B). Capacitances selected as follows (nominal values in μF):

	C_s	C_y	C_o
60 KHz	2000	1600	4800
120 KHz	470	1000	2700


PREAMP
DEMODULATOR
OUTPUT BUFFER
+18 Vreg
1N 5059
2.2K
35μF/25V
100K
820Ω
2.2mH
Cs
Cy
0.01μF
2N3904
eye coil
bias coil
10K
6.8μF
6.8μF
3.3K
3.3K
TP
0.1μF
16 5 15 14
13 5618 12
4 2 3 1 9 8
Co
0.1μF
12K
Cy
0.1μF
adj for
0 V DC
at output
10K
1K
4.7K
4.7K
2N3904
2N3638
6.8K
270Ω
0.1μF
eye position
output Ch 1
AS ABOVE
eye position
output Ch 2

SECTION 2

RAPID EYE MOVEMENTS OF THE CAT

CHAPTER 3

A COMPARISON BETWEEN SACCADES AND QUICK PHASES OF VESTIBULAR NYSTAGMUS IN THE CAT

Status: Submitted to Vision Research

SUMMARY

In alert chronic cats a comparison was made between the time courses of saccades and quick phases of vestibular nystagmus in the horizontal plane. In spite of considerable variability in the time course of these rapid eye movements it appears that saccades and quick phases have identical temporal characteristics. It is shown that there is no linear addition between the oppositely directed slow and quick phase movements during vestibular nystagmus in either light or dark. The results suggest that during the quick phase there is a pause in the signal responsible for generating the slow phase of vestibular nystagmus.

SACCADES AND QUICK PHASES IN CAT

INTRODUCTION

Numerous studies of saccades and quick phases in cat, man, and monkey have demonstrated the existence of specific relations between the amplitude (A), duration (D), and maximum velocity (V) of these rapid eye movements (Fuchs, 1967; Yarbus, 1967; Boghen, Troost, Daroff, Dell 'Osso and Birkett, 1973; Baloh, Sills, Kumley and Honrubia, 1975; Crommelinck and Roucoux, 1976; Collewijn, 1977; Evinger and Fuchs, 1978).

Saccades or quick phases are generated by a pulse of high frequency neural activity, whose duration equals that of the rapid eye movement (Robinson, 1975; Keller, 1977). There is evidence showing that for a given duration the time course of quick phases and saccades in either man or monkey are identical (Ron, Robinson and Skavenski, 1972; Jürgens, Becker and Rieger, 1977). This fact suggests first, that both types of rapid eye movements share a common neural origin; and second, that no addition occurs between the different neural signals responsible for generating the slow and quick phases of vestibular nystagmus. As quick and slow phases are normally in opposite directions, addition of neural signals would result in a reduced velocity and amplitude of each quick phase in relation to a saccade of the same duration. In man and monkey no such change has been observed. Neurophysiological support for this lack of interaction has come from microelectrode recordings in the medial longitudinal fasciculus (MLF) and vestibular nuclei (VN) of alert monkey (Fuchs and Kimm, 1975; King, Lisberger and Fuchs, 1976; Pola and Robinson, 1978). These experiments have suggested that the slow phase

of the vestibulo-ocular reflex (VOR) is mediated by cells in the VN whose discharges pause during quick phases ("tonic-vestibular-pause cells", Pola and Robinson, 1978).

In cat the situation may be different. Although it has been shown that vestibular projections to both the abducens and trochlear nuclei also carry "vestibular-pause" signals (Baker and Berthoz, 1974; Hikosaka, Maeda, Nakao, Shimazu and Shinoda 1977), there is some evidence that quick phases and saccades do not have identical characteristics (Haddad and Robinson, 1977). These authors have reported that, in cat, quick phases are faster than saccades, which suggests an effect opposite to that of linear addition between the quick and slow phases of the VOR.

The present experiments were undertaken to reinvestigate possible differences between spontaneous saccades and vestibular quick phases in the alert chronic cat. Our results show that during whole body, passive rotation quick phases are not faster than saccades. In spite of considerable variability in the time course of these rapid eye movements, our results suggest that saccades and quick phases have identical temporal characteristics in both light and dark.

METHODS

Three cats were first trained to remain relatively immobile for periods of 1-2 hours. Following this initial accommodation period, each animal was anaesthetized with sodium pentobarbital (Nembutal, 30 mg/Kg) and fitted with a surgically implanted scleral eye coil, used subsequently for the recording of eye position (Fuchs and Robinson, 1966; Ferch and Guitton, in preparation). The sensitivity of the system (10 mV/deg for a coil of three turns about the eye) and its frequency response (1 KHz, 3 db) both permitted the resolution of cat eye movements smaller than 15 min arc.

In a subsequent surgical intervention, performed some one to two weeks after the coil implantation, an acrylic implant was fashioned to grip anchor bolts which in turn held the cat's head firmly to the stereotaxic apparatus. While the animal was still anaesthetized, a preliminary calibration of eye position was obtained. The cat's head was placed in the standard position (see below) within the electromagnetic fields of the eye movement recording apparatus. Using a suction contact lens equipped with a stalk, the right (coil equipped) eye was moved passively through $\pm$ 20° in both the horizontal and vertical planes, while respective eye position signals were recorded. The results of this calibration permitted some appraisal of the state of the eye coil implant, and could be compared subsequently with the usual calibration obtained by rotating the field coils through known angles about the stationary eye.

After recovery the alert cat was first fitted into a stereotaxic frame, the horizontal plane of which was tilted to rotate the cat's head 22 degrees downward. In this position the plane of the horizontal semi-circular canals was nearly parallel to the earth's horizontal plane

(Blanks, Curthoys and Markham, 1972) and this was considered to be the cat's normal head posture (Girard, 1930; De Beer, 1947). The field coils were rapidly rotated through accurately predetermined angles in the horizontal plane, relative to the stationary scleral eye coil. This precise calibration could be compared with the horizontal and vertical calibrations obtained earlier.

Records of the horizontal and vertical components of eye movements were made in the light when the animals, with head fixed, looked about spontaneously. Eye movements in the dark were encouraged by providing novel auditory stimuli. Vestibular nystagmus was induced by sinusoidally oscillating the whole animal and surrounding field coils at peak velocities varying between 60^{o}/sec and 10^{o}/sec (see Results) for a peak to peak amplitude of some 45^{o}. The frequency ranged between about 0.1 Hz and 0.45 Hz. Gain of the vestibulo-ocular reflex varied between 0.85 and 0.95 in the light and between 0.60 and 0.90 in the dark. Animals were kept alert by periodically providing small amounts of milk via a gravity fed valve. When the animal was aroused the eye movement records showed a high frequency of spontaneous eye movements and it was during these periods that vestibular nystagmus was induced.

The horizontal and vertical components of each eye movement were recorded on magnetic tape and later played back, for analysis, into a UV mirror galvanometer recorder. For relating amplitude (A), duration (D), and maximum velocity (V) of rapid eye movements, D was determined as the time between the zero velocity points just preceding and following an eye movement (Ron et al., 1972) and V was the maximum slope during the eye movement's time course.

Pure horizontal saccades were not numerous enough to permit

satisfactory statistical analysis. Each population had to be complemented by using oblique saccades which had one largely dominant component in the horizontal direction. The criterion for nearly horizontal saccades was as follows: The amplitude (θ) of an oblique saccade is related to its horizontal (θ_h) and vertical (θ_v) components by the equation

$$\theta = (\theta^2_v + \theta^2_h)^{\frac{1}{2}} \qquad (1)$$

Thus

$$\theta = \theta_h \left(1 + \left(\frac{\theta_v}{\theta_h}\right)^2\right)^{\frac{1}{2}} \qquad (2)$$

In the present work a horizontal saccade was defined as one where

$$\left(1 + \left(\frac{\theta_v}{\theta_h}\right)^2\right)^{\frac{1}{2}} \leq 1.04 \text{ (i.e. max. } 15^o \text{ off the horizontal).}$$

In the data analysis, only the horizontal components of these nearly horizontal saccades were measured.

For each set of eye movements, plots of D vs. A, V vs. A and A vs. D were prepared and linear regression lines were fitted to the data. Saccades smaller than 3^o were not considered so as to avoid the most non-linear portion of each characteristic relation (Yarbus, 1967; Evinger and Fuchs, 1978). Regression lines for saccades and quick phases were compared, to ascertain whether differences between these two types of rapid eye movements were significant. Two regression lines may differ because: (1) their slopes are different; or (2) they have the same slopes but their elevations are different. To test the significance of difference in slopes and elevations, the F-test was used (Snedecor and Cochran, 1968): the results are tabulated (Tables 1 and 2). When the calculated value of

F is equal to or greater than $F_{0.99}$, the probability that the two compared quantities are drawn from a single normal population is less than 1%.

RESULTS

The relations D vs. A and V vs. A for saccades .

Before comparing saccades and quick phases it is of interest to first ascertain whether the present cats performed "normal" eye movements. This can be done by first plotting the durations (D) or velocities (V) of such eye movements as the dependent variables, against the amplitudes (A), and then comparing the characteristics of such D vs. A or V vs. A relations with those obtained by other experimenters. The data available in the literature reveal great variability in both the maximum velocity and duration of saccades of a given amplitude (Stryker and Blakemore, 1972; Crommelinck and Roucoux, 1976; Collewijn, 1977; Evinger and Fuchs, 1978). The measurements of Crommelinck and Roucoux (1976) suggest that almost a two-fold increase in the slope, and a threefold increase in the elevation, of a linear regression line can be caused by changes in alertness from a drowsy to a strongly aroused state. Evinger and Fuchs (1978) however claim that alertness is not the only critical factor.

Table 1 presents a summary of the data obtained in the present experiments, with the number of eye movements, the linear regression equations, and the correlation coefficients given for each of the three cats under the two conditions tested (light and dark). The present untrained cats rarely produced saccades with amplitudes in excess of about 20^{o}. This is compatible with the results of Crommelinck et al.(1977), who showed that the cat's oculomotor range is small and on the average is limited to about $\pm$ 23^{o} from the central position. In the present results, the

relations D vs. A and V vs. A for saccades and quick phases can be represented by linear regression lines with correlation coefficients (r) ranging between 0.20 and 0.77. For these two relations, nearly all values (25 out of 30) of r are significant at better than the 1% level. Three values (double asterisks) are significant at the 5% level, and two (single asterisks) are not significant. The latter two values of r are the lowest and correspond to regression lines fitted to D vs. A relationships. Such large scatter in this data is due to variability in the durations of the saccades' deceleration periods (a similar observation has been made regarding cat saccades by Evinger and Fuchs, 1978; and human saccades by Baloh et al., 1975).

The linear regression lines fitted to the present data vary considerably not only from cat to cat, but occasionally for a specific animal (e.g. cat 3) between saccades measured in the light or dark. For saccades performed in the light, all regression lines, to a good approximation, lie within the extremes given by Crommelinck and Roucoux (1977). They also lie within the range spanned by the two cats of Evinger and Fuchs (1978). In the dark the relation linking duration to amplitude (D vs. A) for cat 3 indicates durations which are particularly long even when compared to those of the drowsy animal. However, this regression line was claculated using only 15 points. Apart from this one exception, the present data can be considered to span the normal range of the cat's saccade characteristics.

Comparison between the characteristics of horizontal saccades and quick phases

Saccades and quick phases may be compared by testing whether their respective regression lines (Table 1), describing D vs. A and V vs. A data, have

significantly different slopes and intercepts. The commonly used D vs. A relation, however, is unsatisfactory for this purpose because neurophysiological observations indicate that a saccade's duration is determined by the duration of a pulse of neural activity (see Keller, 1977, for review), thus suggesting that D should be the independent variable rather than A. The use of the V vs. A relation is also unsatisfactory because any change in V suggests a corresponding change in A (i.e. for a given duration a slower saccade has a smaller amplitude). Thus, even if there were linear addition between slow and quick phase neural signals, individual data points would shift approximately along the V vs. A regression line, resulting in virtually no change in the quick phase V vs. A relation.

For these reasons, it is preferable to take D as the independent variable and to compare saccades and quick phases by using the A vs. D relationship (Jürgens and Becker, 1975). This approach in conjunction with the one used in the next section implicitly assumes that superposition of a low frequency signal (slow phase) unto the high frequency pulse of neural activity determining quick phase duration, will not significantly affect the pulse duration. This point will be considered in more detail in the discussion. Table 1 lists the linear regression equations fitted to the A vs. D data for each of the three cats. Using covariance analysis, two regression lines, describing respectively saccade and quick phase data, may be compared for a given cat, to test whether they have significantly different slopes and/or intercepts (see Methods). The results of comparing A vs. D regression lines for all three animals are shown in Table 2.

For example, line 1 of Table 2 shows a comparison between the regression line through cat 1 A vs. D "saccade in light" characteristic (item 7 of Table 1), and the regression line through the same cat's A vs. D "quick phase in light" data (item 29 of Table 1). The items

compared are given in the extreme left column of Table 2. It can be seen that in all cases there is no significant difference between the slopes of two compared regression lines. For data obtained in the dark there is also no significant difference in common elevation between the lines. In the light, however, there are significant differences in elevation for three of the six cases compared.

Fig. 1 shows a graphical comparison of the regression lines through the A vs. D data for the saccades (SAC, interrupted lines) and quick phases (QP, solid lines) of cat 3. Quick phases were measured while this animal was sinusoidally oscillated at constant amplitude with three different peak velocities, in either the light or the dark. The resulting peak slow phase eye velocities are indicated to the right of each solid line (QP) in Fig. 1. It should be noted that quick phases rarely coincided with the peak slow phase velocity, but were distributed such that the average of all slow phase velocities immediately preceding and following each quick phase, was equal to about 0.60 (S.D. = 0.07) times the peak slow phase velocity. Quantitative comparisons of the saccadic (SAC) regression lines with each of three quick phase (QP) lines are contained in Table 2: Items 9-31, 9-32 and 9-33 (in the light) relate to Fig. 1A, whereas items 18-46, 18-47, 18-48 (in the dark) relate to Fig. 1B. It can be seen that the regression lines for quick phases recorded in the light, with peak slow phase velocities of 59^{o}/sec and 20^{o}/sec, have significantly different elevations from the saccadic (SAC) line; the slopes, however, are similar (comparison of Items 9-31 and 9-33, Table 2). For the situation in the dark, none of the QP regression lines are statistically significantly different from the SAC line, despite the distinctly smaller slope of the 29^{o}/sec QP line. This latter inconsistency is probably a result of the very low (i.e. statistically

not significant) correlation coefficient associated with the 29°/sec QP line (Item 47, Table 1).

Thus, the data of Table 2 indicate that quick phases and saccades recorded in the dark are identical, and that in this condition there is no addition between slow and quick phase signals. However, the results obtained in the light appear conflicting. Even a casual inspection of Figure 1A would suggest that quick phases, recorded at maximum slow phase velocities of 59 and 20°/sec, had consistently smaller amplitudes than saccades of equivalent duration. This could well be consistent with addition of quick and slow phase neural signals during vestibularly induced nystagmus. This possibility is examined in the following section.

Do saccades and vestibular commands add?

Jürgens et al. (1977) have suggested a method of testing for linear addition between the fast and slow eye movements of nystagmus. It consists of computing the difference in velocity between a quick phase and a saccade of similar duration, and comparing this value to the average slow phase velocity associated with that quick phase. This is restated numerically below. A linear regression line can be fitted to A vs. D data for saccades:

$$A_{sac} = A_o + mD \qquad (1)$$

Now, if during a saccadic eye movement a constant velocity ΔV were to be subtracted the resultant quick phase amplitude would be

$$A_{qp} = A_o + mD - \Delta V \cdot D \qquad (2)$$

Rearranging equation (2) and combining with equation (1) yields

$$\Delta V = \frac{A_{sac} - A_{qp}}{D} \qquad (3)$$

This calculated hypothetical slow phase velocity may then be compared to the actual, experimentally determined, slow phase velocity ($\overline{V}_{sp}$): If the two are equal, linear summation exists. Such comparisons are shown, for cat 3, in Fig. 2. Each point in sections A, B, C and D is the result of comparing the mean of the experimentally determined slow phase velocities immediately preceding and immediately following a given quick phase ($\overline{V}_{sp}$), with ΔV. If addition between quick and slow phases had occurred, individual points in each of the four graphs would lie along the dashed lines ($\Delta V = V_{sp}$, slope = 1). In Figs. 2C and 2D, illustrating data obtained in the dark, the points scatter about the abscissae and confirm the covariance analysis of Table 2 (Items 18-46 and 18-48) indicating that no consistent interaction existed between quick phases and saccades. In Fig. 2D the calculated linear regression line (dot-dash line, r = 0.06) through the data points is nearly coextensive with the abscissa and confirms the lack of interaction. In Figs. 2A and 2B the points lie significantly above the abscissae, without however relating to the dashed $\Delta V = V_{sp}$ line. This is again confirmed by the calculated linear regression line (dot-dash, r = 0.06) drawn through the points in Fig. 2B. The fact that most points in Figs. 2A and 2B lie significantly above the $\Delta V = \overline{V}_{sp}$ line suggests that quick phases were consistently slower than could be accounted for by any linear addition of quick and slow phases.

Thus, the above calculations indicate that no linear addition between quick and slow phases of nystagmus occurs, either in the light or the dark. The significant difference that sometimes exists in the light between the

regression lines for saccades and quick phases appears always as a shift in elevation between two parallel lines (Table 2).

DISCUSSION

Characteristics of saccades

The great majority of rapid eye movements recorded from the untrained cats used in this study were less than 20 degrees in amplitude, with a maximum of 25 degrees.

The present results are in agreement with those of previous workers, showing that great variability exists in the duration and maximum velocity of saccades of a given amplitude (Crommelinck and Roucoux, 1976; Evinger and Fuchs, 1978). Two saccades of similar amplitude, occurring close together in time (i.e. < 500 msec), may have significantly different characteristics. Evinger and Fuchs (1978) have concluded that this cannot be explained by changes in the animal's arousal level, as suggested by Crommelinck and Roucoux (1976). In the present results, saccade variability could be partly related to significant variations in the durations of the deceleration phases.

Despite considerable variations, the linear regression equations describing the present V vs. A and D vs. A characteristics of cat saccades lie within the extremes spanning the work of previous authors. This suggests that between one alert cat and another, placed in similar experimental conditions, there can be approximately a two-fold variation in both the slopes and intercepts of the regression lines describing their

saccade characteristics. A comparison of saccades and quick phases, using the physiologically more appropriate A vs. D relation, did not yield more consistent results.

Method used to compare saccades and quick phases

The method of analysis used in this paper was first used by Jürgens and Becker (1975) and Jürgens et al. (1974) to compare saccades and quick phases in man. The procedure assumes that no significant modification of saccade duration occurs if a slow phase signal is superimposed onto the neural signal responsible for the saccade. This hypothesis is suggested by the high frequency pulse-like nature of the saccade signal (Keller, 1977). To verify this hypothesis in cat the calculations leading to the results of Fig. 2 were redone assuming that there was a change in duration due to a superimposed slow phase signal. To do this, hypothetical saccades were obtained by subtracting a ramp (average slow phase during the quick phase) from each quick phase on the eye movement trace. This procedure yielded a saccade whose duration was greater, by some 20% on the average, than that of the original quick phase. The results of Fig. 2 were then recalculated using this new duration. None of the conclusions reached herein were either modified or weakened by this new procedure.

Interaction between the quick and slow phases of nystagmus

Experiments on monkey and man have shown that saccades and the quick phases of vestibular nystagmus have identical characteristics. Therefore, it was concluded that during vestibular stimulation no interaction exists between the slow and quick phase neural signals (Ron et al., 1972; Jürgens et al., 1977). A similar finding has been obtained in man regarding the interaction of smooth pursuit and voluntary saccades. These

findings suggest an interruption of the pursuit signal during the execution of the saccade (Jürgens and Becker, 1975). Surprisingly, Haddad and Robinson (1977) have concluded that cat differs from man and monkey in that the quick phases made during either passive or active head rotation are consistently faster than saccades made with head stationary. The present results obtained during passive whole body rotation are not in agreement with these latter findings.

Thus, in the dark, saccades and quick phases were statistically identical. The significantly slower quick phases demonstrated in about half the cases studied in the light (Fig. 1 and Table 2) cannot be attributed to linear addition between the two neural signals driving the slow and rapid eye movements respectively. In cat 3, for instance, the significant differences between the SAC line and the three QP lines do not seem to be systematically related to the magnitude of the maximum slow phase velocities: quick phase data obtained in the light at the intermediate (44°/sec) velocity are seen to be most closely related to saccades (Fig. 1A). The significant differences that appear between saccades and quick phases at the two extreme (59°/sec and 20°/sec, Fig. 1A) slow phase velocities consist of constant reductions in quick phase amplitudes relative to saccades, regardless of duration (i.e. a downward displacement of parallel regression lines in Fig. 1A; see also Table 2, items 9-31, 9-33). This apparently inconsistent trend in quick phase characteristics suggests the operation of a non-specific influence, such as a change in the level of arousal.

All the evidence quoted so far suggests that for man, monkey, and cat, there is no interaction between the signals generating the slow and

quick phases of vestibularly induced nystagmus either in the light or in the dark. Nevertheless, slow and quick phase interaction does exist under certain conditions. Jürgens et al. (1977) have demonstrated this in human subjects performing targeting saccades while being sinusoidally oscillated in a rotating chair; while Morasso, Bizzi and Dichgans (1973), working with monkeys trained to perform coordinated eye-head movements toward a distinct target, described a reduction in eye saccade velocity by an amount exactly equal to that of the slow phase (head) velocity. It appears, therefore, that goal directed visual target acquisition, and quite possibly mental "set", may play a crucial role in determining whether linear addition of slow and quick phase eye movements will occur.

Neurophysiological correlates

The results of studies using lesions, stimulation and extracellular recording have suggested that saccades and quick phases are generated by identical premotor neural circuits (Cohen and Henn, 1972; Keller, 1977; Nakao et al., 1977).

The manner in which slow and voluntary rapid eye movements interact is not understood. However, the lack of interaction between the rapid and slow phases of vestibular nystagmus does have some neurophysiological correlates. Indeed, recent microelectrode recording from the medial longitudinal fasciculus and vestibular nucleus of alert monkeys have suggested that the vestibulo-ocular reflex is mediated by cells whose discharges pause during quick phases (Fuchs and Kimm, 1975; King et al., 1976; Pola and Robinson, 1978). In cat, microelectrode recordings made from axon terminals of monosynaptic vestibular projections to the trochlear and abducens nuclei have shown that fibres carrying the slow phase (compensatory) signal responsible for driving the agonist muscle,

pause during the (anticompensatory) quick phase when the same muscle becomes the antagonist. Consequently, this implies the absence of summation between slow and quick phase signals on this muscle. However, it is conceivable that such an interaction during the anticompensatory quick phase could occur on the new agonist. Unit recording has revealed nothing on this matter. The present results suggest a lack of interaction between slow and quick phase signals on both the agonist and antagonist muscles responsible for generating the quick phase of vestibular nystagmus during passive whole body rotation.

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Table 1. (Table 3-1)

Linear regression equations and correlation coefficients for duration - amplitude (D vs. A), velocity - amplitude (V vs. A), and amplitude - duration (A vs. D) relations of horizontal saccades and vestibular quick phases. Data were derived from three cats, in both light and dark conditions. A: Saccades. B: Quick phases. Correlation coefficients were significant at better than the 1% level, with the exception of those marked by double asterisks (5%), and single asterisk (not significant). D, A, V, stand for duration, amplitude, maximum velocity, respectively.

TABLE 1

ITEM	EXPERIMENTAL CONDITION	MEASURED QUANTITIES	CAT NO.	PEAK VELOCITY OF SLOW PHASE (°/sec)	NO. OF DATA POINTS	REGRESSION LINE D (msec), A (°) V (°/sec)	CORRELATION COEFFICIENT
A. SACCADES:							
1	Light	D vs. A	1	-	40	D=4.98A + 98.0	0.29*
2			2	-	27	D=3.07A + 63.1	0.58
3			3	-	47	D=4.14A + 54.3	0.53
4		V vs. A	1	-	40	V=8.80A + 20.7	0.57
5			2	-	27	V=11.30A+ 21.1	0.77
6			3	-	47	V=11.52A+ 46.5	0.72
7		A vs. D	1	-	40	A=0.017D+ 4.70	0.29*
8			2	-	27	A=0.109D- 0.93	0.58
9			3	-	47	A=0.069D+ 4.80	0.53
10	Dark	D vs. A	1	-	-	-	-
11			2	-	27	D=4.22A + 67.2	0.69
12			3	-	15	D=9.49A + 65.7	0.63
13		V vs. A	1	-	-	-	-
14			2	-	27	V=7.15A + 40.6	0.73
15			3	-	15	V=4.20A + 62.6	0.49**
16		A vs. D	1	-	-	-	-
17			2	-	27	A=0.113D- 1.83	0.69
18			3	-	15	A=0.042D+ 4.80	0.63

conti. on next page

(TABLE 1 cont'd.)

B. QUICK PHASES:

19	Light	D vs. A	1	30	47	D=5.30A + 102.0	0.35**
20			2	23	48	D=5.50A + 58.9	0.66
21			3	59	42	D=6.10A + 49.5	0.60
22				44	37	D=6.32A + 32.4	0.73
23				20	35	D=9.19A + 49.5	0.68
24		V vs. A	1	30	47	V=8.00A + 17.0	0.61
25			2	23	48	V=7.00A + 42.0	0.65
26			3	59	42	V=8.06A + 44.8	0.60
27				44	37	V=3.98A + 102.3	0.35**
28				20	35	V=3.58A + 58.4	0.57
29		A vs. D	1	30	47	A=0.023D+ 5.44	0.35**
30			2	23	48	A=0.079D+ 0.04	0.66
31			3	59	42	A=0.059D+ 3.81	0.60
32				44	37	A=0.104D- 0.74	0.73
33				20	35	A=0.051D+ 1.91	0.68
34	Dark	D vs. A	1	26	47	D=5.08A + 126.5	0.39
35			2	19	43	D=5.61A + 39.0	0.72
36			3	52	39	D=6.57A + 56.1	0.71
37				29	50	D=2.19A + 124.3	0.20*
38				13	20	D=7.86A + 57.8	0.63
39		V vs. A	1	26	47	V=7.00A + 15.0	0.72
40			2	19	43	V=5.00A + 82.0	0.53
41			3	52	39	V=5.64A + 51.7	0.62
42				29	50	V=8.98A + 8.8	0.72
43				13	20	V=6.44A + 45.9	0.55
44		A vs. D	1	26	47	A=0.030D+ 4.22	0.39
45			2	19	43	A=0.092D+ 1.72	0.72
46			3	52	39	A=0.076D+ 1.40	0.71
47				29	50	A=0.019D+ 7.36	0.20*
48				13	20	A=0.051D+ 2.80	0.63

Table 2. (Table 3-2)

Comparisons between saccades and quick phases: results of covariance analyses, testing the significance of differences between slopes and elevations of the linear regression lines, A vs. D, listed in Table 1. "NO" indicates no significant (0.01 level) difference; whereas "YES" indicates the opposite. The extremen left column indicates what items of Table 1 are compared in the covariance analysis.

TABLE 2

ITEMS COMPARED	EXPERIMENTAL CONDITION	CAT NO.	PEAK VELOCITY OF SLOW PHASE (°/sec)	TEST COMMON SLOPE			TEST COMMON ELEVATION		
				F	$F_{.99}$	Significant at 0.01 level	F	$F_{.99}$	Significant at 0.01 level
7, 29	Light	1	30	0.25	6.93	NO	7.63	6.93	YES
8, 30		2	23	0.96	7.00	NO	6.71	7.00	NO
9, 31		3	59	1.47	6.96	NO	8.9	6.93	YES
9, 32			44	0.07	6.96	NO	3.15	6.96	NO
9, 33			20	3.18	6.96	NO	32.6	6.96	YES
16, 44	Dark	1	26	-	-	-	-	-	-
17, 45		2	19	0.58	7.03	NO	3.10	7.03	NO
18, 46		3	52	1.99	7.17	NO	3.55	7.17	NO
18, 47			29	1.59	7.08	NO	1.81	7.08	NO
18, 48			13	0.15	7.51	NO	0.01	7.51	NO

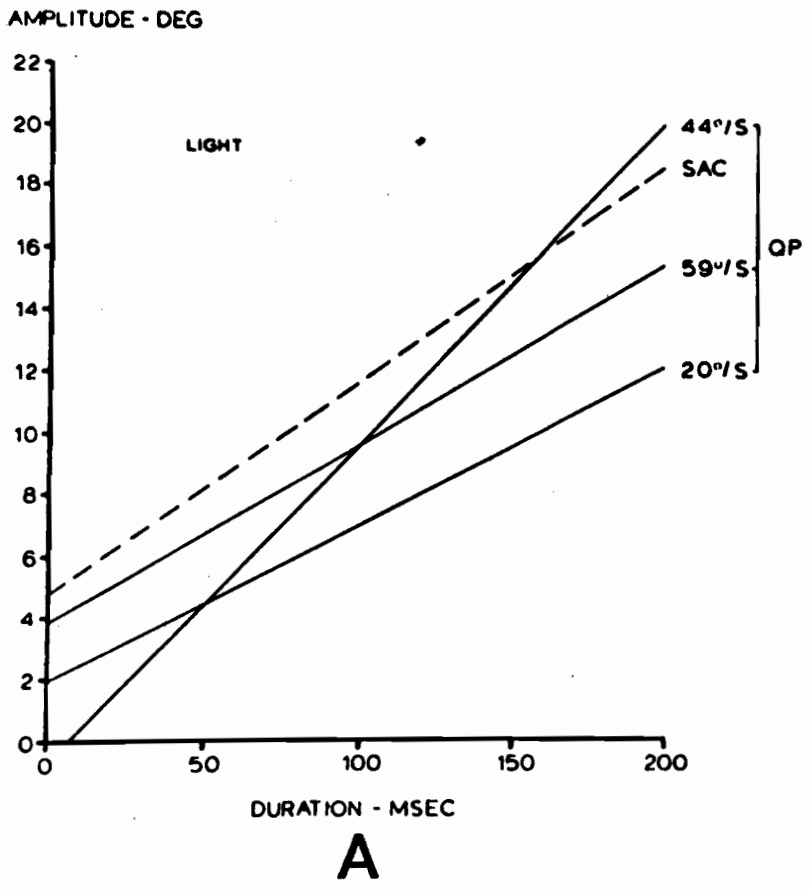
TABLE 2

Fig. 1. (Fig. 3-1)

Regression lines, illustrating the amplitude - duration (A vs. D) relations for spontaneous saccades (SAC, interrupted lines), and vestibular quick phases (QP, solid lines) for cat 3. Quick phase data have been obtained by sinusoidally oscillating the whole animal with head fixed, at frequencies of 0.1, 0.3 and 0.5 Hz. The resulting maximum slow phase eye velocities of 20, 44 and 59°/sec in the light; and 13, 29 and 52°/sec in the dark, are indicated with the QP lines.

A. In the light. For regression line equations and correlation coefficients see Table 1, items 9, 31, 32, 33. Table 2 indicates no significant differences in slopes between SAC and QP. Significant differences in elevation between SAC and QP exist for peak slow phase velocities of 20 and 59°/sec, but not for 44°/sec.

B. In the dark. See Table 1, items 18, 46, 47, 48. Table 2 indicates no significant differences in slopes or elevations between SAC and QP.


AMPLITUDE - DEG
LIGHT
44°/S
SAC
59°/S
20°/S
QP
DURATION - MSEC
A

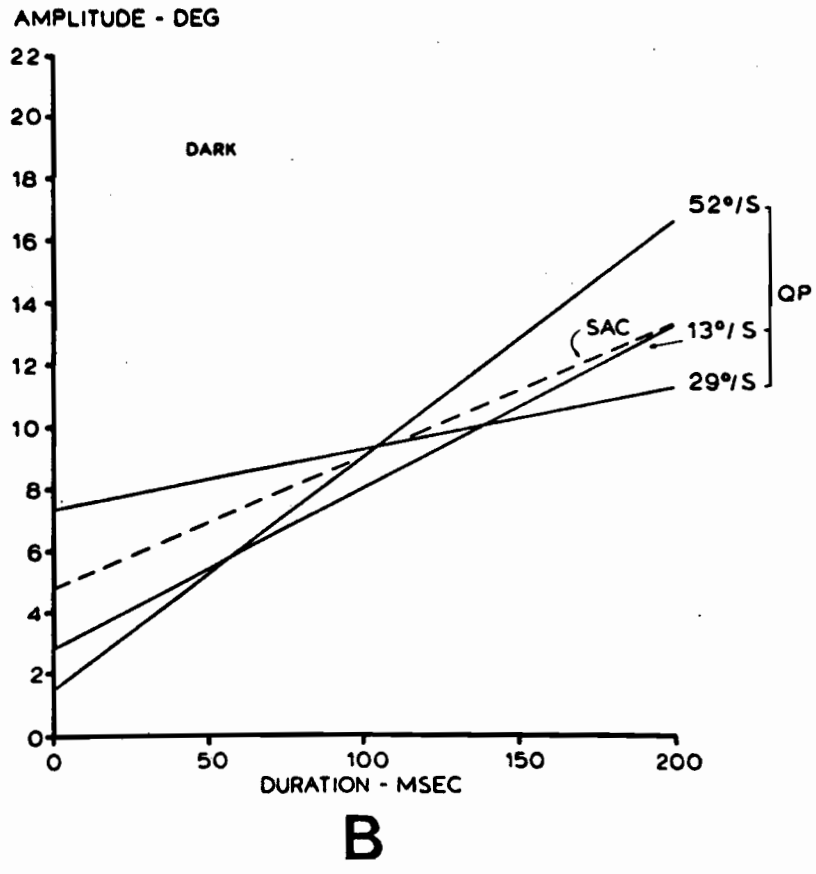
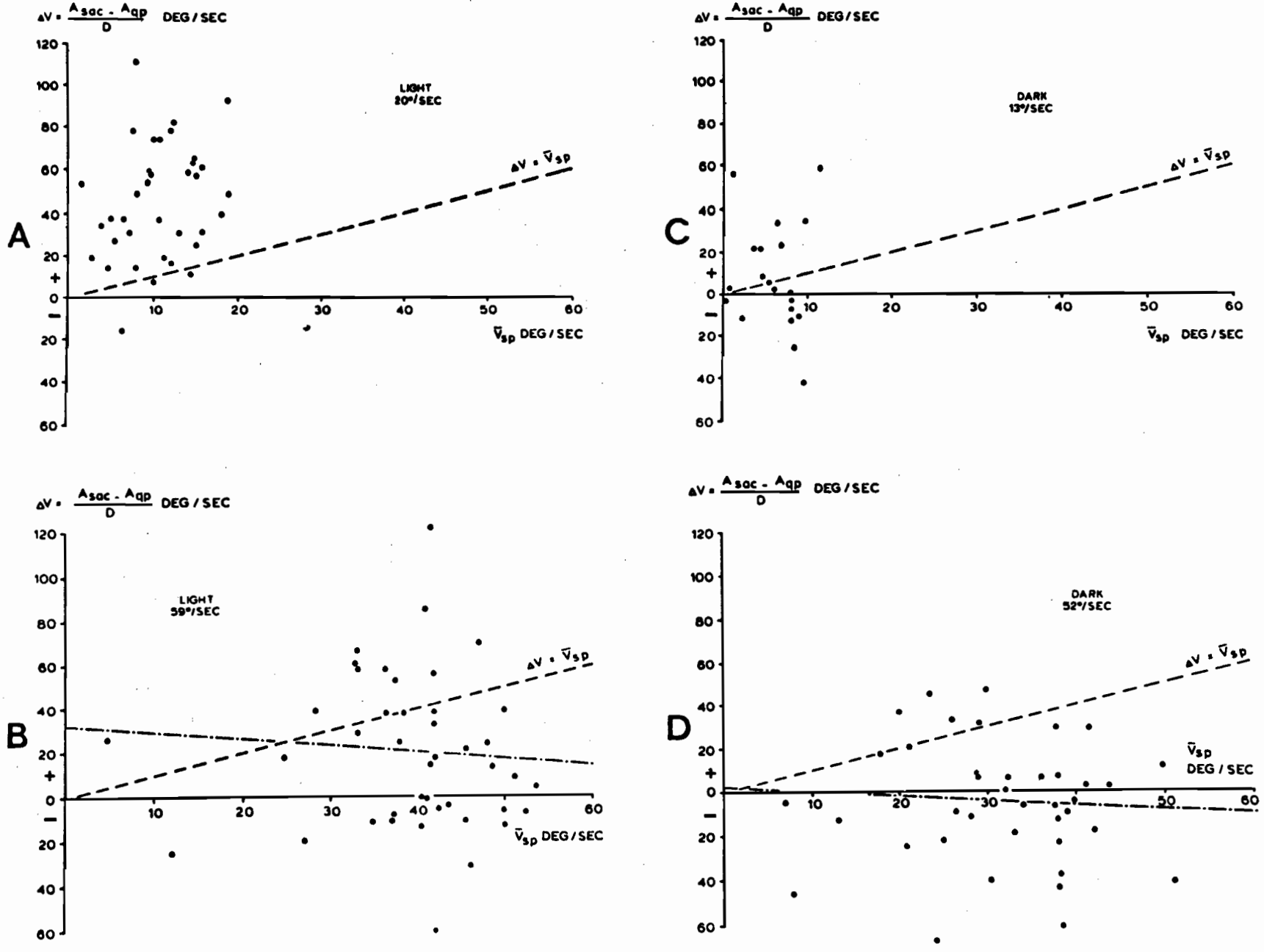

AMPLITUDE - DEG
DARK
52°/S
SAC
13°/S
29°/S
QP
DURATION - MSEC
B

Fig. 2. (Fig. 3-2)

Comparisons of ΔV with $\overline{V}_{sp}$. ΔV is the difference between the maximum velocity of a voluntary saccade and the maximum velocity of a quick phase of equal duration; $\overline{V}_{sp}$ is the mean value of the slow phase velocities immediately preceding, and immediately following, a given quick phase. If linear summation of slow and quick phase velocities were taking place, individual data points would lie along the interrupted lines (i.e. $\Delta V = \overline{V}_{sp}$). Data points above these lines indicate quick phase velocities slower than those predicted by linear summation, whereas points below these lines indicate velocities faster than predicted. A_{sac}: saccade amplitude (deg). A_{qp}: quick phase amplitude (deg). D: duration (sec). A,B. In the light. The frequency of oscillation was 0.1 Hz, with a peak slow phase eye velocity of 20°/sec (A); and 0.5 Hz with 59°/sec (B). C,D. In the dark. For a frequency of 0.1 Hz, peak slow phase eye velocity was 13°/sec (C); for 0.5 Hz it was 52°/sec (D).


A
ΔV = (A sac - A qp) / D DEG / SEC
LIGHT
20°/SEC
ΔV = V̄sp
V̄sp DEG / SEC
C
DARK
13°/SEC
B
LIGHT
59°/SEC
D
DARK
52°/SEC
V̄sp
DEG / SEC

CHAPTER 4

OBLIQUE SACCADES OF THE CAT: A COMPARISON BETWEEN THE DURATIONS OF HORIZONTAL AND VERTICAL COMPONENTS

Status: Submitted to Vision Research

SUMMARY

A comparison was made between the durations of the orthogonal components of oblique saccades made by cats in the light and dark, and the durations these components would have if they existed alone as pure movements. It was found that on the average there was a significant increase in the duration (stretching) of the short component of nearly horizontal and nearly vertical saccades in both of these conditions. Stretching was nevertheless incomplete. On the average the short component in the light was stretched such that its duration was 90% that of the main component. In the dark, stretching of the short component also occurred but was significantly less on the average (75%) because there frequently occurred non-stretched components.

OBLIQUE SACCADES IN CAT

INTRODUCTION

There is considerable physiological and anatomical evidence suggesting that two separately located neural circuits are responsible for the immediate supranuclear control of horizontal and vertical saccades (Büttner-Ennever and Henn, 1976; Henn and Cohen, 1976; Büttner, Büttner-Ennever and Henn, 1977; Keller, 1977; King and Fuchs, 1977; Büttner-Ennever and Lang, 1978). This observation in conjunction with the fact that vertical and horizontal eye movements require different combinations of extra-ocular muscles, suggests that the characteristics of saccades in these orthogonal directions might be different. In man, Yarbus (1967) has shown that only a very small difference exists between horizontal and vertical saccades with the latter having a slightly longer duration. In contrast to this result, Evinger and Fuchs (1978) have shown that, in cats trained to orient towards a visual target, vertical saccades have a shorter duration and are faster than horizontal saccades of the same amplitude.

Most saccadic eye movements, however, are not restricted to either the horizontal or vertical planes, but rather consist of oblique movements having components in each of the two planes. It is still unclear how these orthogonal components of oblique saccades are coordinated. Bahill and Stark (1975, 1977) have concluded that in man the horizontal and vertical components of oblique saccades are totally independent dynamically and most probably also temporally. Nevertheless, 40% of the components of their oblique saccades had no temporal independence and were reported to begin and end at nearly the same time. In trained cats, Evinger and Fuchs (1978) have shown that on the average

the short component (say 3^{o} horizontal) of an oblique saccade has a duration which is longer than that of an equivalent pure movement (i.e. a pure 3^{o} horizontal saccade). In this paper we have tried to determine, in untrained cats, the extent and frequency of this "stretching" of the short saccadic component, and the dependence of such "stretching" on whether the oblique saccades are performed in the light or in the dark.

METHODS

The methods have been described in the preceding paper (Guitton and Mandl, preceding paper). In brief, eye movements in two cats were recorded using the eye coil in magnetic field technique (Ferch and Guitton, in preparation). Care was taken to assure that orthogonality existed between the two magnetic fields required to detect horizontal and vertical eye movements. This was verified by either inducing a cat to track a target moving horizontally, or rotating the field coils in the horizontal plane, and verifying that no signal appeared on the vertical eye movement channel.

Records of the horizontal and vertical components of eye movements were made in the light, when the animals with heads fixed looked about spontaneously or tracked small targets of interest; or in the dark, when they looked about spontaneously, frequently in response to unusual noises. In addition, animals were kept alert by periodically providing small amounts of a favourite liquid via a gravity fed valve. When suitably aroused, the animals exhibited a high frequency of spontaneous eye movements.

Duration/amplitude (D vs. A) and velocity/amplitude (V vs. A)

relations for horizontal as well as vertical saccades were plotted, and linear regression equations derived. The duration (D) of a saccade was taken as the time between the zero velocity points just preceding and following an eye movement (Ron et al., 1972). Occasionally a rapid eye movement was followed by an unusually long deceleration period (a "glissade"). In such cases, the duration was taken as the time between the points where the amplitude of the saccade was 95% completed. The maximum velocity of a saccade was determined by measuring the maximum slope during its time course.

The regression lines of D vs. A and V vs. A of horizontal saccades were compared with those for vertical saccades using covariance analysis and the F-test (Snedecor and Cochran, 1968; Guitton and Mandl, preceding paper). A similar analysis was used to compare the durations of the horizontal and vertical components of oblique saccades.

RESULTS

Comparison between pure horizontal and vertical saccades in the light

It is well known that the time course of cat saccades can be described by characteristic relations expressed as linear regression equations linking duration (D), or maximum velocity (V) with amplitude (A), (Crommelinck and Roucoux, 1976; Evinger and Fuchs, 1978; Guitton and Mandl, preceding paper).

Table 1 contains the linear regression equations applicable to pure horizontal and vertical saccades made by each of the two cats in the light. In each animal the correlation coefficients were higher for the V vs. A than for the D vs. A data. This is because the deceleration

period following the point of maximum velocity frequently varied between saccades of the same amplitude (Evinger and Fuchs, 1978; Guitton and Mandl, preceding paper).

The linear regression equations are plotted in Fig. 1. It can be seen that in cat 2 the vertical saccades are faster than the horizontal ones. For cat 3, and over most of the range of amplitudes, the opposite is true. As the characteristics of cat saccades are highly variable (Crommelinck and Roucoux, 1976; Evinger and Fuchs, 1978; Guitton and Mandl, preceding paper), the significance of the differences between the characteristics of horizontal and vertical saccades was tested using covariance analysis. For each cat, the V vs. A and D vs. A relations for horizontal saccades were compared with the homologous relations determined for the vertical movements. The results, given in Table 2, indicate that, for both animals, no significant difference exists between horizontal and vertical saccades, as determined by comparing the slopes of either the D vs. A or the V vs. A, regression lines. However, in one of the two cats a significant difference does exist between horizontal and vertical saccades, as determined by comparing the elevations of either the D vs. A, or the V vs. A, regression lines.

Oblique saccades: comparison between the duration of horizontal and vertical components

In the preceding section, the characteristics of pure horizontal or vertical saccades were described. Consider now an oblique saccade of say 15° amplitude directed 20° up. For this eye movement the horizontal and vertical components should be equal to about 14° and 5°, respectively. If these components remain independent and retain the characteristics of their respective pure horizontal and vertical movements, then according

to Fig. 1A, and say cat 2, the duration of the horizontal component should be some 106 msec, and that of the vertical component some 67 msec. The possible existence of such a predicted difference in the duration of the horizontal and vertical components of an oblique saccade can easily be verified experimentally.

To do this, we have selected from both cats two groups of oblique saccades whose directions in both the light and dark, ranged between 10^{o}-33^{o} (mean, $\overline{\theta}_1 = 24^{o}$, S.D. 7.1) and 55^{o}-75^{o} (mean, $\overline{\theta}_2 = 67^{o}$ S.D. 9.3), relative to the horizontal. Saccades of all available amplitudes were included within these two groups, providing they met the directional criteria. Within each group, the durations of the horizontal and vertical components were obtained. These are shown plotted for both cats in Fig. 2, for saccades performed in a normally lit room (2A) and in total darkness (2B). The solid line at 45^{o} indicates where the points should lie if for each point the duration of the vertical component equalled that of the horizontal component: i.e. if $D_v = D_h$. This is true for only a small number of points. In fact, 82% of all points related to saccades in both light and dark, whose mean duration is 24^{o} ($\overline{\theta}_1$) lie below the 45^{o} line; whereas 68% of all points related to a mean direction of 67^{o} ($\overline{\theta}_2$) lie above the line. Comparing the data in Fig. 2A (in the light), with those in Fig. 2B (in the dark), indicates that the points in the latter graph, corresponding to either $\overline{\theta}_1$ or $\overline{\theta}_2$, show a lesser degree of correlation with the 45^{o} line than those of the former. To illustrate the difference between light and dark, linear regression lines were fitted to the points corresponding to the nearly horizontal oblique saccades ($\overline{\theta}_1$). These are shown in Fig. 2 (dashed lines). The equations are:

light: $D_v = 0.86\ D_h + 5.5$; $r = 0.94$ (1)

dark : $D_v = 0.66\ D_h + 12.7$; $r = 0.86$. (2)

Covariance analysis revealed a significant difference (1% level) between the interceptsof these lines, but not between their slopes. Thus in the dark as compared to light there was a significantly greater independence between the durations of horizontal and vertical components of oblique saccades.

The above regression equations fitted to the $\overline{\theta}_1$ data emphasize that on the average, in both light and dark, the smaller of the two orthogonal components of an oblique saccade has a shorter duration than that of the longer component. The same is true for the data corresponding to nearly vertical saccades ($\overline{\theta}_2$, filled symbols) although in this case the regression line (not shown) fitted to the "light" data is nearly coextensive with the line $D_v = D_h$. In spite of the fact that the short component has a duration smaller than that of the horizontal, it is still possible that there has been an increase in its duration relative to that of a pure movement of the same amplitude. The extent of this possible stretching is considered below.

"STRETCHING" of the short component

If the horizontal and vertical components remain totally independent, the predicted average relation between D_v and D_h can be determined from the regression equations linking D with A and given in Table 1.

For horizontal and vertical saccades one can write

$$D_h = m_h A_h + b_h \qquad (3)$$

$$D_v = m_v A_v + b_v \qquad (4)$$

where subscripts "h" and "v" signify horizontal and vertical, respectively. Consider all saccades directed $\overline{\theta}^{o}$ from the horizontal,

$$\frac{A_v}{A_h} = \tan \overline{\theta} \qquad (5)$$

combining equations (3) to (5) and assuming, based on the covariance analysis of Table 2, that $m_v = m_h$, yields

$$D_v = D_h \tan \overline{\theta} + (b_v - b_h \tan \overline{\theta}). \qquad (6)$$

It is now possible, by substituting the appropriate values of b_v and b_h, to determine for each cat the predicted average relation between D_v and D_h. For illustrative purposes the calculations presented below will be made for the data represented by the open symbols ($\overline{\theta}_1$) of cat 2. The data obtained from cat 3 yielded identical results.

For cat 2, $\overline{\theta}_1 = 23^{o}$. Inserting the values of b_v and b_h from Table 1, and $\overline{\theta}_1$, into equation (6) yields

$$D_v = 0.42\, D_h + 28.0 \qquad (7)$$

This equation is shown plotted in Figs. 3A and 3B (dot-dash lines) along with the data of cat 2 for both the "in-light" and "in-dark" conditions, respectively. The extreme limits of the straight line are determined

by the limits of the linear regression lines, D vs. A, shown in Fig. 1 for cat 2.

If there were total independence between the horizontal and vertical components of the oblique saccades, the data points should lie scattered about the line given by equation 7. In the dark (Fig. 3B) the points do exhibit such a tendency although most points lie clustered nearer to the $D_v = D_h$ relationship. In the light (Fig. 3A) the points lie well away from equation 7, suggesting a high degree of temporal dependence between D_v and D_h for these nearly horizontal ($\overline{\Theta}_1 = 23^o$) oblique saccades.

This apparent dependence between the horizontal and vertical components in either light and dark for cat 2 can be verified statistically by calculating the confidence limits (Snedecor and Cochrane, 1968) on the regression equation fitted to the open symbols. These equations, and the confidence limits (probability level of 0.001) are:

light (cat 2) $D_v = 0.83\ D_h + 8.71$ (dashed line, Fig. 3A)

$0.61 < \text{slope} < 1.06$

dark (cat 2) $D_v = 0.76\ D_h + 2.49$ (dashed line, Fig. 3B)

$0.38 < \text{slope} < 1.14$

Thus, in the light the probability appears to be extremely low that the slope of the regression line through the open data points of Fig. 3A, should equal 0.42 (equation 7). In the dark the probability is somewhat greater though still insignificant.

It follows from the above analysis that in both light and dark the

short component of an oblique saccade is significantly stretched; though not sufficiently to equal the duration of the main component.

The degree of stretching that the short component has undergone may be conveniently stated by giving the slope of the regression line through the origin. For the data points obtained in the light (Fig. 3A, open symbols).

$$D_v = 0.93\ D_h,$$

and therefore on the average the short component of this family of oblique saccades is stretched such that its duration is 93% that of the long component. In the dark (Fig. 3B, open symbols) the stretching has been shown to be significantly less and is given by

$$D_v = 0.79\ D_h$$

Similar conclusions apply to the filled symbols corresponding to the nearly vertical saccades ($\overline{\theta}_2$) of cat 2 as well as to the data of cat 3.

DISCUSSION

The results obtained from the two cats studied in the present experiments suggest that on the average vertical and horizontal saccades in cat are identical. In contrast, the two cats studied by Evinger and Fuchs (1978) had vertical saccades that were faster and shorter than saccade of equivalent amplitude in the horizontal plane. In man, Yarbus (1967) has reported that vertical saccades are slower than horizontal ones.

Horizontal and vertical saccades are driven by different sets of extraocular muscles. There is also considerable physiological and anatomical evidence suggesting that two separately located neural circuits are

responsible for the immediate supranuclear control of horizontal and vertical saccades (Büttner-Ennever and Henn, 1976; Henn and Cohen, 1976; Büttner, Büttner-Ennever and Henn, 1977; Keller, 1977; King and Fuchs, 1977; Büttner-Ennever and Lang, 1978). The question of how the horizontal and vertical components of an oblique saccade are coordinated is therefore of particular interest. It appears from the work of Bahill and Stark (1975, 1977) that in man these orthogonal components are dynamically independent. By this is meant that there is independence of the magnitudes and time courses of the two orthogonal forces acting on the eye ball. The nature of the temporal dependence of these force components - i.e. their relative onset times and durations - is less clear. Bahill and Stark (1977) have reported that 40% of oblique saccades have orthogonal components that begin and end almost simultaneously. The results of Viviani, Berthoz and Tracey (1977) suggest that the duration of the horizontal component is always consistently shorter. The present work has been concerned only with a comparison of durations in cat.

For complete temporal <u>in</u>depencence, each orthogonal component should have a duration identical to that of a pure (horizontal or vertical) movement of the same amplitude; this duration should be determined by the linear regression equation describing the amplitude-duration relationship. Conversely, for complete temporal dependence, both components should have identical durations. Bahill and Stark (1977) have pointed out that "a great deal of computational effort would be necessary to create this very tight crosslinking of the horizontal and vertical channels: the duration of the smaller component would have to be stretched

out by a very precise amount ...".

There are neurophysiological observations which suggest that the orthogonal components of oblique saccades should have equal durations. There is a class of neurons in the monkey's brainstem called "omnipausers" whose high frequency spontaneous discharge pauses during saccades in all directions (Keller, 1977). According to a model proposed by Robinson (1975), the duration of the pause in the "omnipauser" cell's activity determines the duration of a saccade and, by extension of this hypothesis, the duration of each of the components of an oblique saccade. In support of this, Henn and Cohen (1973) have claimed that the horizontal and vertical components of a monkey's oblique saccade have equal duration.

The experiments of Evinger and Fuchs (1978) have shown that in 25-40% of the cases there is stretching of the short component of an oblique saccade performed by a trained cat acquiring a visual target. The extent of this stretching was not considered. The present results have shown quantitatively that there was significant stretching of all short components (D_v) of oblique saccades directed, in the light, at angles varying between 10° to 30° off the horizontal ($\overline{\theta}_1$, Figs. 2A and 3A). Stretching was nevertheless incomplete. For one cat the short component was stretched such that $D_v = 0.93\ D_h$ and on the average for the two cats, $D_v \approx 0.9\ D_h$. By contrast, in the dark, stretching of the short component of an equivalent family of saccades occurred, but on the average was significantly less because there frequently occurred non-stretched components. Stretching in the dark was given by $D_v = 0.79\ D_n$ for cat 2 and on the average for both cats was $D_v \approx 0.75\ D_h$. Similar

results were obtained for the nearly vertical oblique saccades.

Evinger and Fuchs (1978) have suggested that stretching of the short component may be caused by either neural or peripheral effects. If the cause were peripheral, it would hardly be expected that two oblique saccades having similar amplitudes and directions could in one case have a stretched component (say, in the light) and in another case (say, in the dark) have components that are independent (see inset of Fig. 2B). Such a variation was found in the present results. Bahill and Stark (1977) have stated that stretching, when seen in humans, seems associated with short components having an exaggerated length of their deceleration period. This "glissadic" shape (Weber and Daroff, 1972) results from what is called a pulse - step mismatch (Robinson, 1975). Despite the fact that this type of saccade is seen frequently in cat (Evinger and Fuchs, 1978), examination of the present eye movement records of oblique saccades performed in the light has <u>not</u> revealed many short saccadic components with unexpectedly long deceleration periods (see inset of Fig. 2B). This suggests that stretching of the short component is probably caused by an increase in the duration of the neural pulse responsible for the generation of the short saccadic component, relative to the value it would have if it were to generate a pure movement of the same amplitude. Appropriate pulse-step matching in this case, would require a lower discharge frequency within the stretched pulse. Such a reduced frequency would result in a lower than expected velocity of the short component and this is actually observed(Evinger and Fuchs,1978).

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Table 1. (Table 4-1)

Linear regression equations and correlation coefficients for duration - amplitude (D vs. A), velocity - amplitude (V vs. A) relations of horizontal and vertical saccades made in the light. Data were derived from two cats. A: Horizontal saccades. B: Vertical saccades. Correlation coefficients were significant at better than the 1% level. D, A, V, stand for duration, amplitude, and maximum velocity, respectively.

TABLE 1

ITEM	SACCADE CHARACTERISTICS	CAT NO.	NUMBER OF POINTS	REGRESSION LINE	CORRELATION COEFFICIENT
A. HORIZONTAL					
1	D vs. A	2	27	D= 3.07A + 63.1	0.58
2		3	47	D= 4.14A + 54.3	0.53
3	V vs. A	2	27	V=11.30A + 21.1	0.77
4		3	47	V=11.52A + 46.5	0.72
B. VERTICAL					
5	D vs. A	2	32	D= 2.75A + 54.4	0.64
6		3	18	D= 2.26A + 86.6	0.23
7	V vs. A	2	32	V=12.4 A + 43.4	0.79
8		3	18	V=15.37A - 30.1	0.70

Table 2. (Table 4-2)

Comparisons between horizontal and vertical saccades: results of covariance analyses, testing the significance of differences between slopes and elevations of the linear regression lines, D vs. A and V vs. A listed in Table 1. The extreme left column indicates what items of Table 1 are compared in the covariance analysis. "NO" indicates no significant (0.01 level) difference; whereas "YES" indicates the opposite.

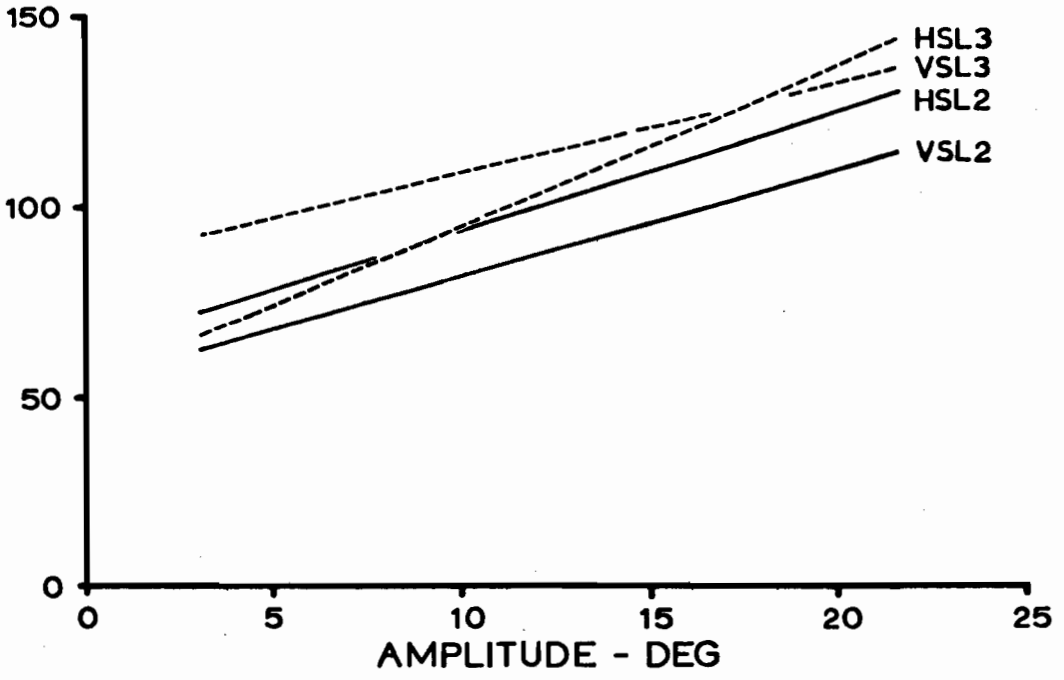
TABLE 2

ITEMS COMPARED	SACCADE CHARACTERISTICS	CAT NO.	TEST COMMON SLOPE			TEST COMMON ELEVATION		
			F	$F_{.99}$	Significant at 0.01 level	F	$F_{.99}$	Significant at 0.01 level
1,5	D vs. A	2	0.10	7.12	NO	8.92	7.11	YES
2,6		3	2.06	7.08	NO	0	7.07	NO
3,7	V vs. A	2	0	7.12	NO	11.20	7.11	YES
4,8		3	0.97	7.08	NO	1.26	7.07	NO

Fig. 1. (Fig. 4-1)

Regression lines illustrating duration - amplitude (D vs. A, Fig. 1A), and maximum velocity - amplitude (V vs. A, Fig. 1B) relations for "pure" horizontal and vertical saccades. HSL, VSL: horizontal and vertical saccades in the light, respectively. Numbers refer to cats named 2 and 3.

A


DURATION - MSEC
150
100
50
0
0
5
10
15
20
25
AMPLITUDE - DEG
HSL3
VSL3
HSL2
VSL2

B

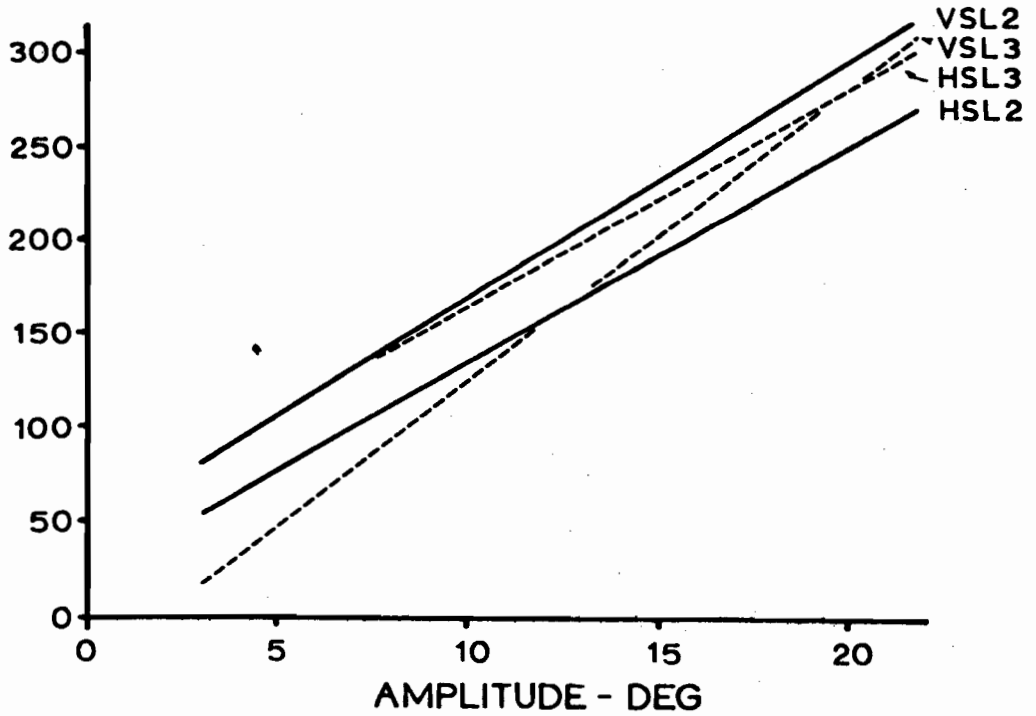
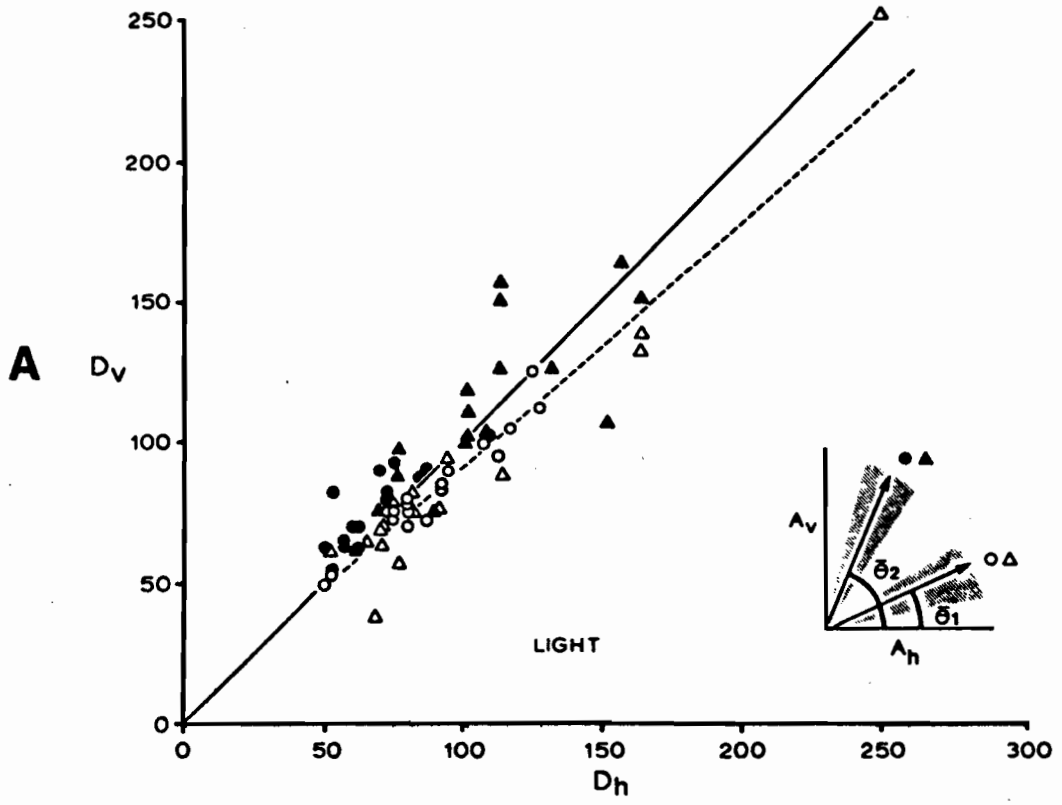

MAXIMUM VELOCITY
DEG / SEC
300
250
200
150
100
50
0
0
5
10
15
20
AMPLITUDE - DEG
VSL2
VSL3
HSL3
HSL2

Fig. 2. (Fig. 4-2)

A comparison between the durations of horizontal (D_h) and vertical (D_v) components of oblique saccades. A. In the light. B. In the dark. In each condition two groups of oblique saccades were selected (see inset, Fig. 2A): those with mean directions of 24° relative to the horizontal ($\bar{\theta}_1$, range 10°-33°, open symbols); and those with mean directions of 67° relative to the horizontal ($\bar{\theta}_2$, range 55°-75°, filled symbols). The solid line at 45° indicates where each point should lie if for a given oblique saccade, the duration of the vertical component equalled that of the horizontal. The dashed lines are the linear regression lines through the open symbols, and are given by equations 1 and 2. The inset of Fig. 2B shows examples of "unstretched" (upper part, note difference in durations of H and V components) and "stretched" (lower part) short components. The data were obtained from two cats: ○, ●, cat 2; △, ▲, cat 3. D_h and D_v are in msec.


A
D_V
250
200
150
100
50
0
0
50
100
150
200
250
300
D_h
LIGHT
A_V
$\bar{\sigma}_2$
$\bar{\sigma}_1$
A_h

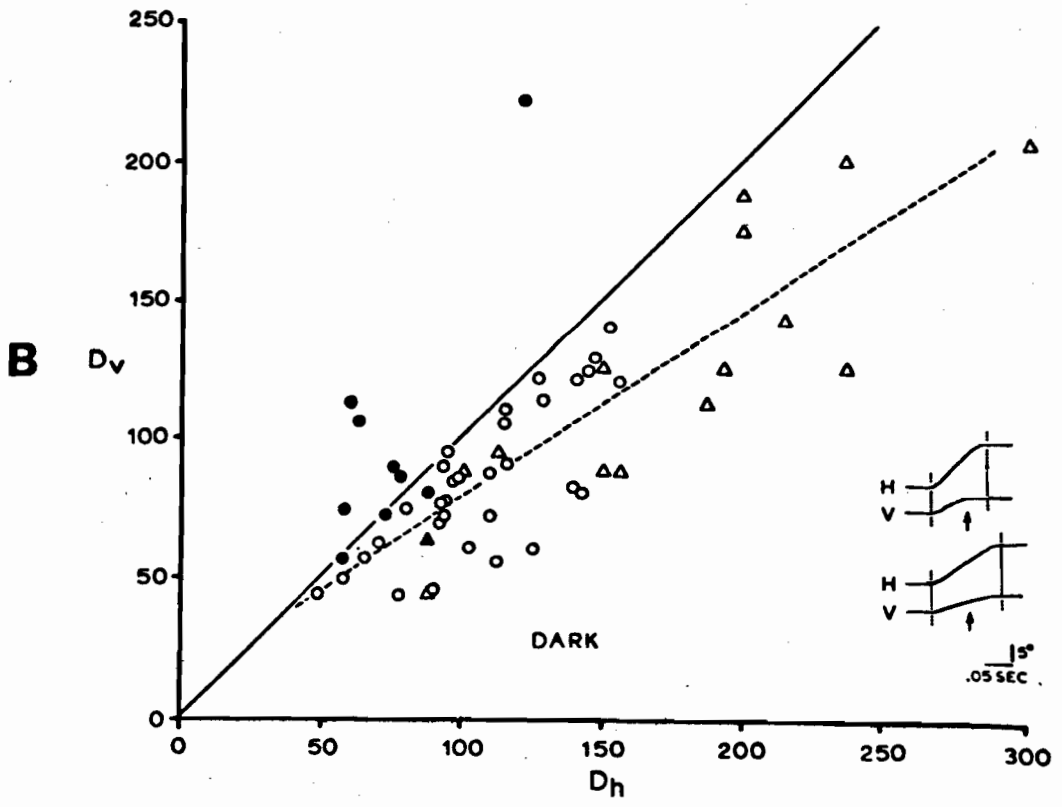
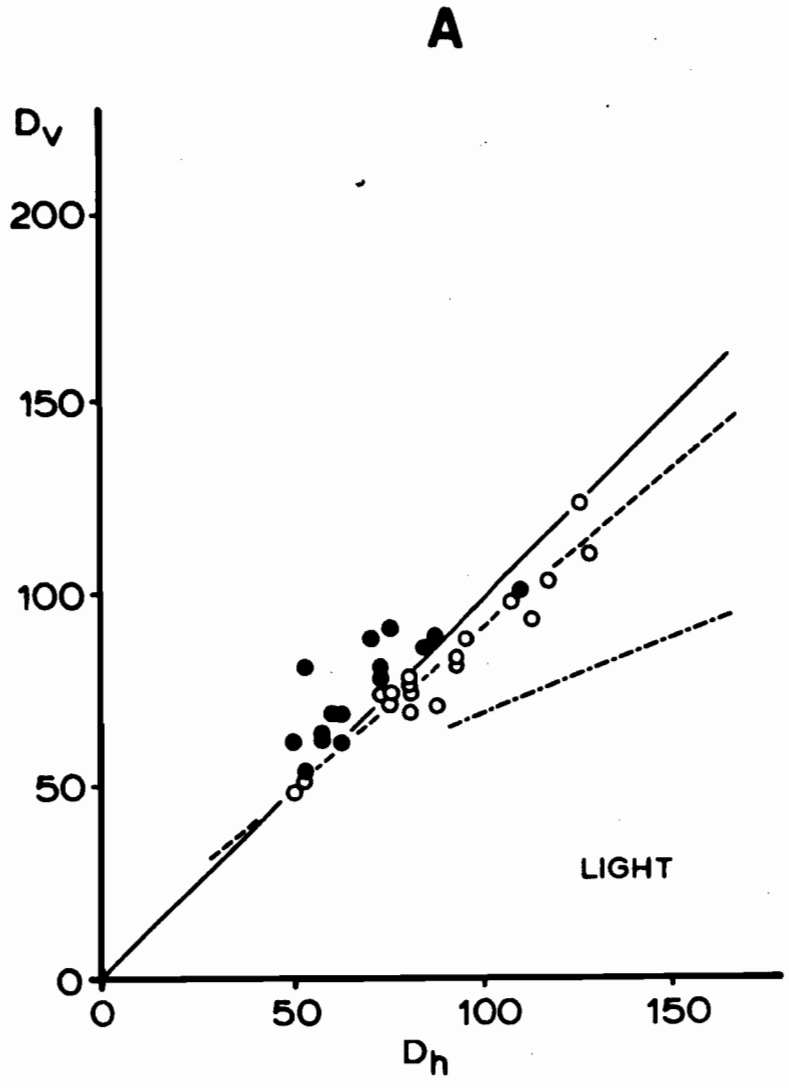
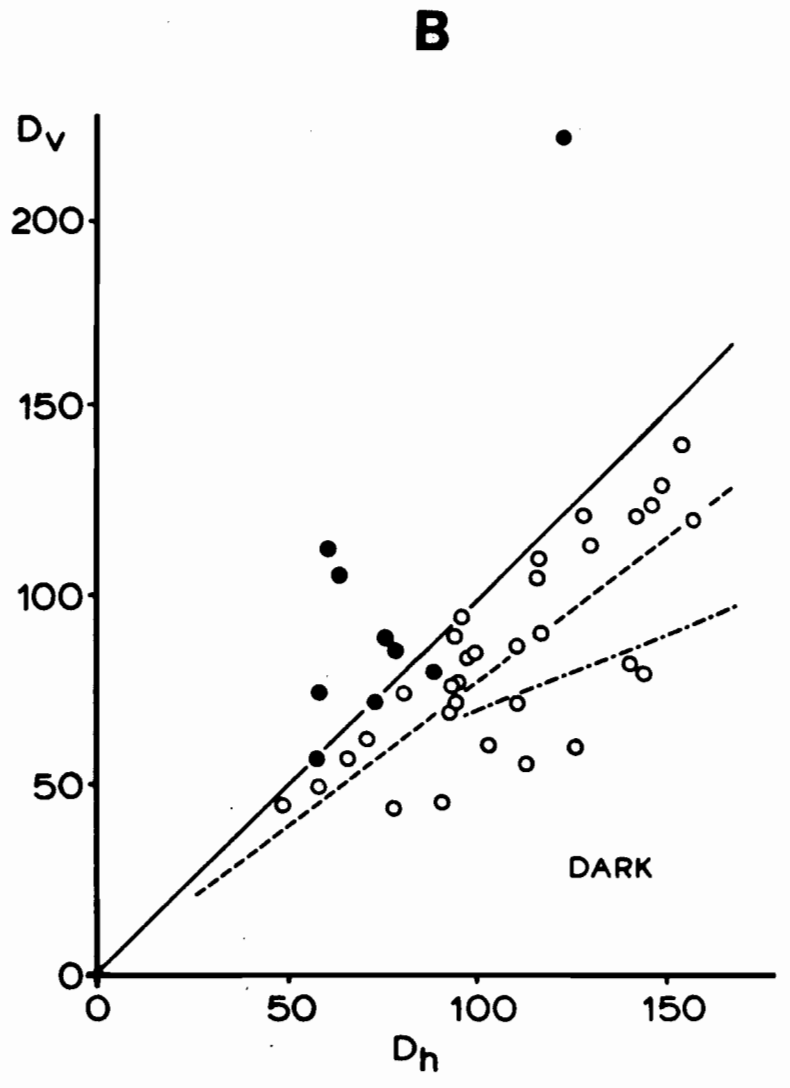

B
D_V
250
200
150
100
50
0
0
50
100
150
200
250
300
D_h
DARK
H
V
H
V
5°
.05 SEC

Fig. 3. (Fig. 4-3)

A comparison between the durations of horizontal (D_h) and vertical (D_v) components of oblique saccades for cat 2. A. In the light. B. In the dark. The dashed lines are the linear regression lines through the open symbols. The dot-dash lines represent the predicted relation between D_v and D_h if total independence existed between the horizontal and vertical components; i.e. if each component retained the duration it would have if it existed alone as a "pure" movement. Note that in the light the points lie closer to the line defining the relation $D_v = D_h$. Open symbols: oblique saccades having a mean direction 23^o off horizontal. Closed symbols: oblique saccades having a mean direction 67^o off horizontal. See legend to Fig. 2 for additional details. D_h and D_v are in msec.


A
D_V
200
150
100
50
0
0
50
100
150
D_h
LIGHT


B
D_V
200
150
100
50
0
0
50
100
150
D_h
DARK

SECTION 3

CORTICAL CONTROL OF EYE MOVEMENTS:

THE ROLE OF THE FRONTAL EYE FIELD

CHAPTER 5

THE FRONTAL EYE FIELD IN MAN AND MONKEY: AN OVERVIEW OF CONTEMPORARY KNOWLEDGE

THE FRONTAL EYE FIELD (FEF) IN MAN AND MONKEY

More than 100 years have passed since Ferrier (1874) and Hitzig (1874) reported that eye movements could be elicited by stimulating parts of the frontal lobe of monkey. The excitable region became known as the FEF. Subsequent early studies of this phenomenon concentrated on delineating the region of excitable cortex; describing its cytoarchitectural characteristics; specifying the effects of stimulation; and describing the behavioural effects of ablation. These early studies have been reviewed somewhat generally by Holmes (1938) and in great detail by Smith (1949) and Brucher (1964). With the gradual refinement of techniques, the earlier cruder experiments using stimulation were subsequently repeated; some afferent and efferent fibre systems were described; more sophisticated behavioural testing was applied before and after ablation; and finally unit recordings were made while monkeys surveyed the visual scene. These later physiological studies have been reviewed by Jeannerod (1972) and the anatomical data by Nauta (1971). The present short discussion will concentrate primarily on contemporary discoveries.

The FEF is usually considered to be part of the frontal lobe because its thalamocortical afferents arise in the mediodorsal thalamic nucleus (Nauta, 1971). The FEF is situated in a transition zone, with agranular motor cortex lying posterior, and the granular cortex forming the expanse of the frontal lobe lying anterior (Akert, 1964). This intermediate "dysgranular" region (Nauta, 1971) of the cortex occupies a territory whose cytoarchitectural definition is not wholly agreed upon (Astruc, 1971; Smith, 1945), but which is generally considered to be nearly

coextensive with Brodmann's area 8.

Very recent attempts to localize the FEF in man have been made by measuring the increase in regional cerebral blood flow, associated with the performance of saccadic eye movement (Melamed and Larsen, 1979). Results are generally in agreement with previous results of Penfield (see Melamed and Larsen, 1979) and suggest that the FEF occupies portions of Brodmann's areas 8, 6 and 4. (Interestingly the present work, described in chapters 6 and 7, has reached a similar conclusion regarding the localization of the FEF in the cat).

In monkey the FEF, as defined by electrical stimulation, is situated in the periarcuate region. The anatomical connections of this area have been the subject of numerous studies and the complexity of the circuitry is noteworthy. The following is a simplified summary of the afferent and efferent connections. (A summary, to 1971, of frontal lobe connections has been given by Nauta, 1971).

Afferent projections from cortex to the FEF appear to arise in the: (1) dorsal bank of the principal sulcus of the frontal lobe; (2) visual association areas 18, 19 and MT; (3) somatosensory association area 5 of the parietal lobe; and (4) auditory association areas in the caudal portion of the superior temporal gyrus (Pandya and Kuypers, 1969; Jones and Powell, 1970; Pandya, Dye and Butters, 1971; Spatz and Tigges, 1972; Chavis and Pandya, 1974; Kaas, Lin and Wagor, 1977).

Among the subcortical afferents to the monkey FEF there are projections arising in medial pulvinar (Trojanowski and Jacobson, 1974), nucleus medialis dorsalis (MD) of the thalamus (Akert, 1964;Kievits and Kuypers, 1975) and in the claustrum (Riche and Lanoir, 1978).

Efferent projections from FEF have been the subject of a number of studies. Among the more recent investigations are those of Kuypers and

Lawrence (1967); Pandya and Kuypers, 1969; Pandya and Vignolo, 1971; Astruc, 1971 and Künzle and Akert (1977). The latter and latest work is in general agreement with previous workers, and will be summarized below. Künzle and Akert (1977) have shown that FEF sends ipsilateral projections to: (1) a more anterior region on the dorsal bank of the principal sulcus; (2) area 7 of the parietal lobe; (3) the superior temporal sulcus; (4) the caudate nucleus; (5) thalamic nuclei, especially MD; (6) the pretectal region; (7) the superior colliculus (SC); and (8) nuclei of the pons (griseum pontis and nucleus reticularis tegmenti pontis). Spatz (1976) has shown that the FEF also projects to area MT.

In summary, the FEF exhibits reciprocal connections with (1) a frontal region on the dorsal bank of the principal sulcus; (2) cortical association areas implicated respectively in the processing of visual, auditory and somatosensory information; and (3) the thalamic nucleus MD. Moderate to heavy subcortical projections arising from the periarcuate area, are directed to the SC and the pontine grey. It is noteworthy that, in monkey, no projection has been found in regions of the midbrain or pons that are thought to contain the immediate supranuclear neural circuits responsible for generating horizontal or vertical eye movements (Cohen and Henn, 1972; Büttner et al., 1977; Keller, 1977; King and Fuchs, 1977).

There has been great interest in the FEF. If its functional role could be understood, it seems reasonable to believe that this would yield important clues to frontal lobe function in general. Furthermore, the FEF has classically been considered to be the cortical oculomotor area. Indeed it has been known for some time that unilateral FEF ablation results in immediate neglect of objects in the contralateral visual field;

a deviation of the head and eyes to the side of the lesion (ipsilateral side), and an incapacity to perform voluntary saccades towards the contralateral hemifield (Kennard and Ectors, 1938). Bilateral ablation results in a fixed gaze directed straight ahead and, transiently, there are no voluntary eye movements (Kennard and Ectors, 1938). The hypothesis that the FEF is the cortical oculomotor area has been further strengthened by noting its proximity to motor cortex, its contribution to the pyramidal tract (Bizzi, 1968; Kuypers and Lawrence, 1967) and the characteristics of eye movements evoked by focal stimulation (Robinson and Fuchs, 1969).

Stimulation of the FEF in monkey has been shown to yield eye movements whose characteristics are indistinguishable from normal voluntary saccades (Robinson and Fuchs, 1969). Stimulating a cortical point evokes a saccade of a specific amplitude and direction. The great majority of stimulated sites yield contralateral eye movements and the shortest latency between the onset of the stimulus and that of the saccade is 15 msec. On the basis of the observation that stimulation of the third nerve evokes eye movements with a 5 msec latency, Robinson and Fuchs (1969) argued that the pathways from FEF to brainstem must be closely coupled to the oculomotor nuclei. (The "all or nothing" saccadic response precludes a direct monosynaptic link). There is a heavy projection from the FEF to the SC (Astruc, 1971; Künzle et al., 1976) and saccadic eye movements organized in the brainstem (Cohen and Henn, 1972; Raybourn and Keller, 1977) might be triggered by impulses travelling there via the FEF-SC pathway. However, in monkey this is not so, for two reasons. First, stimulation of the FEF evokes eye movements with shorter latencies than does stimulation of SC (15 vs. 20 msec; Robinson,

1972; Robinson and Fuchs, 1969). Second, eye movements can still be elicited from the FEF when the SC has been ablated (Schiller, 1972). Therefore, the pathway mediating eye movements evoked by FEF stimulation in monkey probably bypasses the SC and reaches the pons via a more direct route (Astruc, 1971; Künzle and Akert, 1977).

The role of the FEF-SC projection remains totally enigmatic. It has been argued that FEF stimulation may, after all, only elicit eye movements via an axon reflex; i.e. by exciting collaterals of brainstem neurons implicated in oculomotor control. This would also conveniently explain why neurons discharge after the onset of eye movement (see below). A test of this hypothesis remains to be made.

Despite: (1) the early behavioural deficits; (2) the short latency between an applied stimulus and the evoked saccade; and (3) the close coupling between FEF efferents and oculomotor nuclei; there is strong evidence which shows that the FEF is <u>not</u> a cortical oculomotor area. This evidence comes primarily from observations that neurones which discharge in association with saccades do so only <u>after</u> the initiation of the eye movement (Bizzi, 1968; Bizzi and Schiller, 1970; Mohler, Goldberg and Wurtz, 1973). By contrast, in motor cortex many cell discharges precede a movement (Evarts, 1966). Other evidence comes from the observation that the early behavioural deficits following FEF ablation are transient and animals eventually are capable of making saccadic and smooth pursuit movements in response to visual stimuli (Holmes, 1938; Crosby, Yoss and Henderson, 1952; Henderson and Crosby, 1952; Latto and Cowey, 1971 a and b, and 1972; Pribram, 1955). Furthermore, as pointed out by Künzle and Akert (1977), the "output circuits of the frontal eyefield have little in common with motor and premotor cortical

areas ... Instead, they follow the basic pattern of frontal granular cortex, with one possible exception, namely the absence of limbic and hypothalamic connections."

The study of the long-lasting deficits following FEF ablation has been instrumental in providing new hypotheses regarding FEF function. The enduring disorders described to date include: (1) the tendency to perseveratively track and fixate visual targets (Holmes, 1938; Jeannerod, 1972; Smith, 1949); (2) amblyopia (Kennard and Ectors, 1938; Latto and Cowey, 1971 a and b); and (3) a reduced ability in unpractised visual search (Latto and Cowey, 1972; Latto and Iversen, 1973).

In light of current knowledge, the amblyopia is perhaps the least surprising of these impairments. The FEF is intimately connected, via numerous pathways, with primary visual association areas (see discussion above). Furthermore, nearly half of the recorded neurones in the FEF have been reported to respond to visual stimulation without ever discharging in association with eye movements (Mohler et al., 1973). Many of these visual responses are enhanced whenever the animal makes a saccade to fixate the visual stimulus (Wurtz and Mohler, 1976 b). The discharge properties of such neurons in the FEF resemble those of units in the SC (Goldberg and Wurtz, 1972), and suggest that the FEF like the SC may play a role in the mechanisms controlling selective attention (Mohler and Wurtz, 1976; Wurtz and Mohler, 1976 a).

The observation of perseverative fixation and tracking led Holmes (1938) some forty years ago to suggest that the FEF was necessary for the purposeful scanning of the environment, where attention, discrimination, and recognition are necessary to select and fixate relevant visual targets. In monkey, recently found deficits in visual search (Latto and Cowey,

1972; Latto and Iversen, 1973) seem closely related to this view. Holmes postulated that the FEF possessed "the power of inhibiting inappropriate and undesirable activities of the occipital lobe" mediated via the occipito-tectal pathway. The demonstrated pathway from FEF to SC (Astruc, 1971; Künzle et al., 1976), plus evidence showing that stimulation of the FEF can modify the discharge characteristics of SC cells (Guitton and Mandl, 1974; 1976; and Chapter8) yield anatomical and physiological evidence which lends some credence to Holmes' hypothesis. The relationship between perseverative behaviour, frontal lobe function and inhibitory fronto-brainstem pathways is a common theme that has recurred in many studies. For example, recently Moll and Kuypers (1977) have shown that ablation of the premotor cortex in monkey (including the FEF) "impairs the capacity of the contralateral arm to reach around a transparent obstacle to a visible food reward and results in a tendency of the arm to reach straight to where the food is visible."

Inhibition of occipital cortex, mediated by FEF, has been proposed by Henderson and Crosby (1952) to explain why heightened and sustained optokinetic responses occur following bilateral destruction of the FEF. The inhibitory role of the FEF has also been considered by Jeannerod (1972) in relation to frontal lobe function. Denny-Brown (1958) has discussed equilibrium of cortical responses, and a disturbance of this equilibrium resulting in "transcortical release" when one region is destroyed.

Unfortunately the notion that the FEF suppresses or prevents the release of a perseverative tracking behaviour is difficult to interpret in the light of the finding that single units discharge only <u>after</u> the initiation of saccades. Other hypotheses of FEF function have been

proposed which are more compatible with this observation. For example, it has been suggested that the FEF monitors eye movements (Latto and Cowey, 1971 a and b). This hypothesis is also compatible with the presence of single units in the FEF that code eye position (Bizzi, 1968; Bizzi and Schiller, 1970). It has also been suggested that the FEF is the source of the "corollary discharge" discussed in Chapter 1 (Teuber, 1960). The timing of FEF unit burst discharges in monkey seems compatible with the modification of some unit discharges in the SC during eye movements (Robinson and Wurtz, 1976). A test of this hypothesis has shown that although these collicular units do receive an extra-retinal input, FEF ablation does not modify their discharge characteristics (Wurtz, private communication). It is noteworthy, also, that units have been recorded in the FEF that discharge in association with and precede head movements (Bizzi and Schiller, 1970). However, no further experiments have considered the possibility that the FEF may be implicated in head motor control.

Despite the great attention that has focused on the link between the FEF and oculomotor control, it should not be forgotten that this cortical region has been reported to receive multimodal afferent projections (Pandya and Kuypers, 1969; Jones and Powell, 1970; Nauta, 1971). Furthermore, there are a number of reports describing long-lasting deficits other than oculomotor or visual. For example, Goldman and Rosvold (1970) have shown that arcuate lesions impair performance on an auditory conditional position discrimination in which the type of response depends on the spatial location of the auditory signal. More recently, Petrides and Iversen (1976) have shown that a lesion of the banks and depth of the arcuate sulcus induces a long-lasting impairment

of cross-modal matching whereby an animal that has learned a discrimination by touch cannot now discriminate by visual inspection alone.

Despite evidence suggesting an involvement of the FEF in multimodal tasks - which is compatible with the apparent multimodal inputs - it should be borne in mind that this cortical region may not be a homogeneous area. Chavis and Pandya (1974) have reported that the different primary association areas relating to visual (areas 18 and 19), somatosensory (area 5) and auditory (the caudal part of area 22) inputs project to different zones about the arcuate sulcus. Furthermore, the experiments of Wurtz and Mohler (1976 b), involving unit recording in the FEF of alert monkeys, have suggested a heterogeneous distribution of the visually responsive, and eye-movement related, cells recorded in this periarcuate region.

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CHAPTER 6

FRONTAL 'OCULOMOTOR' AREA IN ALERT CAT: I. EYE MOVEMENTS AND NECK ACTIVITY EVOKED BY STIMULATION

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SUMMARY

(1) Stimulation within cat frontal lobe elicited saccadic eye movements whose maximum velocity was significantly greater than that of normal spontaneous saccades.

(2) The majority (90%) of stimulated cortical points yielded eye movements whose directions and amplitudes were independent of the position of the eye in the orbit. The direction of these eye movements depended on the site being stimulated, with a discrete and orderly representation of directions existing within the cortex.

(3) A lesser number of cortical points (10%) yielded centering movements whose directions and amplitudes depended on the position of the eye in the orbit, rather than on the site being stimulated.

(4) Evoked neck muscle activation frequently preceded evoked eye movements by some 15-30 msec. This timing was compatible with a coordinated head-eye orientating response.

(5) On the basis of the directions, and the latencies, of evoked eye movements, the cat frontal oculomotor area could be divided into two subregions, a 'medial' and a 'lateral'.

(6) The 'medial' area included the mesial wall of the hemisphere with a portion of the lower lip of the cruciate sulcus, and the medial wall of the presylvian sulcus. This area yielded contraversive eye movements with shorter latencies (average 45 msec).

(7) The 'lateral' area included primarily the lateral wall of the presylvian sulcus. It yielded predominantly centering eye movements, and ipsiversive movements with longer latencies (65 msec).

(8) The functional characteristcs of the 'medial' area, as revealed by focal stimulation, resembled those of the monkey frontal eye field.

EYE MOVEMENTS AND NECK ACTIVITY EVOKED BY STIMULATION OF FEF

INTRODUCTION

It is well known that electrical stimulation, applied to a specific region of the human and simian frontal lobe, can elicit conjugate saccadic eye movements that are usually accompanied by head movements[34,40,47]. This cortical region is referred to as the frontal eye field (FEF) and corresponds closely to Brodman's area 8. Classically, it has been regarded as the cortical oculomotor center, but the discovery that unit discharges follow, rather than precede, the onset of saccadic eye movements[6] has discredited this hypothesis.

The existence of a corresponding area in the cat's frontal lobe has been suggested in numerous studies[5,15-17,22,31-33,35,45,46], but there has been little agreement regarding its anatomical location. The detailed works of Hassler[29] and Schlag and Schlag-Rey[43] suggest that eye and head movement in cat can be obtained by stimulating portions of: (i) the lower lip of the cruciate sulcus; (ii) the mesial wall of the hemisphere; (iii) cortex surrounding the presylvian sulcus; and (iv) an excitable strip of frontal cortex linking the latter two regions[29,43]. Hassler's experiments also suggested that evoked eye and head displacements in the cat acted synergistically, resulting in a coordinated orienting movement similar to that observed when stimulating the FEF of monkey[10].

While this information on cat suggests the existence of a frontal region implicated in eye and head movement control, it does not provide firm evidence for a functional homology with the monkey FEF. Indeed, there is some evidence suggesting that no such homology exists: (i) neither the mesial nor the presylvian 'oculomotor' regions in cat are coextensive with any of the suggested but still debated boundaries of area 8[28,30,45,52], and (ii) the majority of evoked saccades in cat have been reported to return

the eye to a central position in the orbit[43], whereas in monkey, localized FEF stimulation elicits saccades whose amplitudes and directions are nearly constant and independent of the initial eye position[40].

The situation is further complicated by the fact that, compared to monkey, there is a paucity of electrophysiological data available about the cat's frontal 'oculomotor' region. There has as yet been no detailed quantitative study of eye movements evoked by stimulation in chronic awake and alert cats, nor is there any information available regarding the relation of single unit activity to spontaneous eye movements. In the studies of Schlag and Schlag-Rey[43], and Hassler[29], eye movements were visually observed and, in the former work, encéphale isolé preparations were used.

The experiments to be described in this and the following paper were performed on normal alert cats and had two general objectives. The first was to describe the properties of those single unit discharges in the frontal lobe that accompany voluntary eye movements and changes in neck EMG. The results of that work are described in the following paper[26]. The second objective was to record, in a precise and quantitative way, eye movements and associated neck EMG activity elicited by focal threshold stimulation at points where unit discharges had just been recorded. This second series of experiments is described in the present paper.

METHODS

Experimental results were drawn primarily from 3 of the 6 tested female cats.

Eye movement recording

Eye movements were recorded using the electromagnetic technique first described by Robinson[38]. The transducer which sensed eye movements was a coil of wire implanted about the eye. This coil moved with the eye, and an electromotive force (e.m.f.) that varied with eye position was induced in the windings by two orthogonal, spatially fixed, but rapidly alternating magnetic fields. The electronic circuitry controlling the magnetic fields, and demodulating the eye coil signal, used frequency coding rather than phase coding as used by Robinson[38], and will be described extensively elsewhere[18]. The sensitivity of the system (10 mV/degree for a coil of 3 turns about the eye) and its frequency response (1 kHz, 3dB) both permitted the resolution of cat eye movements as small as 15 min arc. The maximum field intensity near the animal's head was 10 mgauss, which was 3 orders of magnitude less than that reported to have effects on behaviour[19].

Animal preparation

Surgery was performed during two separate sessions. Each cat was anaesthetized with sodium pentobarbital (Nembutal, 30 mg/kg). In the initial session, three turns of 0.0085 in. (215 μm) diameter, 7 strand, teflon coated steel wire (Medwire Corp., Mt. Vernon, N.Y., U.S.A., part no. 316SS7/44T) were implanted about the animal's right eye, using the method of Fuchs and Robinson[21]. A neck EMG electrode, consisting of a piece of the same wire formed into a hook and bared at the tip (3 mm), was thrust into the left biventer cervicis muscle guided by a hypodermic needle.

Final surgery, providing access to the right frontal lobe, was performed some 5-6 days before an animal was to begin the recording sessions. The frontal 'oculomotor' area in cat lies in the depths of the frontal lobe, and it is most conveniently localized by using distances measured from the cruciate sulcus. The relative coordinates are given by Schlag and Schlag-Rey[43]. A stainless steel well was fitted over an opening in the skull overlying the cruciate sulcus, and dental acrylic poured over the dried exposed bone so as to cover anchor bolts which had previously been attached to the skull. Threaded sleeves designed to attach the cat's head were also anchored to the acrylic implant. The well was filled with an antibiotic solution (0.25% neomycin sulphate) and firmly capped.

While the animal was still anaesthetized, a preliminary calibration of eye position was done. The cat's head was placed in the standard position within the electromagnetic fields of the eye movement recording apparatus. Using a suction contact lens equipped with a stalk, the right eye was moved passively through known angles in both the horizontal and vertical planes, while respective eye position signals were recorded. The results of this calibration permitted some appraisal of the state of the eye coil implant, and could be subsequently compared with the calibrations obtained by displacing the field coils through known angles (see below).

Experimental procedure

The alert implanted cat was first fitted into a loosely fitting cloth bag and then inserted into a plastic tube whose axis was set parallel to the mid-line of the stereotaxic frame. The stereotaxic horizontal of the frame was tilted to rotate the cat's head 22^{o} downward. In this position the plane of the horizontal semicircular canals was parallel to the earth's horizontal plane[8], and this was considered to be the cat's normal head

posture[14,23]. The field coils were positioned such that the cat's implanted right eye was in the center of the magnetic fields.

A reference gaze axis was defined by an imaginary straight line running parallel to the stereotaxic sagittal and horizontal planes and passing through the center of the implanted eye. This line has been shown to be nearly coincident with the cat's central gaze axis[12]. The axis intersected a white cardboard tangent screen placed some 50 cm in front of the cat. At this point of intersection a small hole was pierced in the screen and a small black rod was poked through. As the alerted animal fixated the rod, the signals coding horizontal and vertical eye positions were recorded on magnetic tape. This procedure identified the central gaze axis and was repeated before and after every recording session. As the cat fixated the rod, the field coils were also rapidly rotated through accurately predetermined angles in the horizontal plane. This precise calibration could be compared with the calibration obtained during anaesthesia.

With the animal's head fixed by the stereotaxic apparatus, an exploratory tungsten stimulating microelectrode (impedance 50 kΩ at 60 Hz) was first introduced via the well to a point permitting access to either the mesial or presylvian regions[43]. While the electrode was being lowered in successive 0.5 mm steps, a standard pulse train (pulse width 500 μsec; frequency 200/sec; train duration 60 msec) was applied using a current of 300 μA. When a depth was reached where stimulation evoked either eye movements or changes in biventer cervicis EMG, the exploratory stimulating electrode was withdrawn and was replaced by a high impedance (10 MΩ at 60 Hz)

microelectrode with its tip at the position last stimulated. This new electrode was further advanced in search of single unit activity related to spontaneous eye movements. When such a unit was found, the changes in its activity associated with eye movements and neck muscle activity were studied in detail[26]. Subsequently, with the same electrode in place, a systematic stimulation procedure was begun. While the animal looked spontaneously about the lighted room, the standard stimulus train was applied with a current of 100 μA. The horizontal and vertical components of the eye movements, the evoked EMG from biventer cervicis, and the stimulus marker pulses were recorded on four track magnetic tape during time intervals of 3 minutes. At selected points the current threshold was tested (about 50 μA; see Results), and the effect of increasing the current to 100, 200 and 300 μA was determined. Evoked eye movements were also tested when the animal looked about spontaneously in the dark, and while it was tracking a moving target. On the average, 10 penetrations were made in every animal over a one month period.

During the tests, it sometimes happened that cats became drowsy and fell asleep. To prevent this, and to encourage arousal, all cats were fed milk at intervals during the experiment.

At the end of the last experimental session an animal was anaesthetized and the points where relevant unit activity had been recorded[26] were marked by passing current through a stainless steel microelectrode (Prussian blue method). The brain was then fixed by perfusion and embedded in paraffin. Serial sections were cut every 25 μm and stained with cresyl fast violet. The electrode tracks were located and reconstructed by identifying the relevant blue spots.

Using a small computer, approximately 500 evoked saccades were analysed. Each eye movement was reconstructed vectorially from the horizontal and vertical components, and plotted on a polar diagram whose center corresponded to the cat's reference gaze position. The amplitude, direction, and latency of saccades evoked at a given point were averaged. Average amplitudes and directions from all cats were plotted on enlarged representative coronal brain sections taken from one of the animals.

Relevant portions of neck EMG records were rectified, frequency modulated and averaged using a small special purpose averaging computer.

RESULTS

Eye movement vectors related to cortical sites

Stimulation of well defined regions within the frontal lobe of alert cats evoked two types of rapid conjugate ocular displacements. With one type, both amplitude and direction of an evoked saccade were constant and independent of the initial position of the eye in the orbit. With the other type, stimulation evoked saccades directed approximately towards the center of the cat's oculomotor range, and therefore the amplitude and direction depended on the initial position of the eye.

With eye movements of the first type, mean amplitudes and directions were calculated and the resulting vectors drawn to scale on appropriate coronal sections through the frontal pole (Fig. 1). The tail-end of each single arrow indicates the site where the electrical stimulation was applied. Other symbols are explained in the figure caption. The cortical sites where eye movements could be elicited corresponded well with those described by Schlag and Schlag-Rey[43] (save for the lower lip of the cruciate sulcus) and Hassler[29]. Fig. 1 reveals that, contrary to results obtained in

monkey, a topographical distribution of evoked eye movement directions exists within the frontal lobe of cat. This distribution was found to be consistent between animals. Contralateral movements with an upward component were obtained primarily from the mesial cortex. The direction of these movements changed from nearly horizontal in the mesial cortex at the rostral end (section B) to nearly vertical some 4 mm posterior (section E).

The cortex surrounding the presylvian sulcus has the shape of an inverted U. In the superior and inferior parts the dominant directions were upward and downward, respectively (sections A-C). The upward movement became progressively more ipsilateral as the electrode descended the lateral wall (section B). In both the medial and lateral limbs of the U the change in direction from upward to downward was quite abrupt. The transition point in the lateral limb of section A was characterized by complex eye movements composed of upward and downward displacements.

Centering movements were observed during stimulation of the more posterior regions, and were elicited primarily from the lateral wall of the presylvian sulcus (sections C and D), and from a few points in the lower lip of the cruciate sulcus (sections A and D).

Fig. 2A shows examples of evoked eye movements that are generally of similar amplitude and direction, in this case up and towards the left (contralateral). Nevertheless, if the eye starts down-right, the displacement tends to have a somewhat greater amplitude; and if the eye is down-left or up-right, the evoked eye movements tend to converge slightly. A similar phenomenon has been reported in monkey during stimulation of either the FEF[40], or the superior colliculus[39]. The eye movements shown in Fig. 2A were evoked by stimulating the mesial wall of the hemisphere (Fig. 1C), at a point coincident with the tail of the uppermost arrow. The vector at this

point represents an average amplitude of 4.9° (S.D. ± 2.0) and an average direction of 33.4° (S.D. ± 14.6) with respect to the horizontal. Such standard deviations are typical of those calculated for other stimulated points.

Fig. 2B shows examples of centering movements, elicited from the lateral wall of the presylvian sulcus (Fig. 1C). The eye movements did not reach a well defined, small area within the visual field, but their "goal" lay close enough to the center of the oculomotor range to suggest a form of gaze centering.

The two categories of ocular displacements illustrated in Figs. 2A and 2B appear distinct. Nevertheless, the experimental verification of this in untrained animals was problematic, because it was frequently difficult to evoke eye movements whose starting points were distributed evenly throughout the visual field.

Time course of evoked eye movements

The insets in Fig. 3 show the time courses of two typical spontaneous saccades compared with those of two evoked eye movements. It can be seen that, despite similar amplitudes, the evoked saccades are considerably faster than the spontaneous ones. This comparison can be made more general by noting that for man, monkey and cat, specific functional relationships have been established that link the amplitude of spontaneous saccades with their duration and maximum velocity[3,9,13,20]. In cat the most consistent relation is that between maximum eye movement velocity and amplitude[13]. These quantities are plotted in Fig. 3, for both evoked and normal exploratory saccadic eye movements in the alert animal. It can be seen that the evoked movements are consistently faster than the spontaneous ones. This has also been shown by Crommelinck[11] who stimulated the superior colliculus of cats.

Latencies of evoked eye movements

In two cats a statistical comparison was made between the latencies of the up, down, contraversive and ipsiversive components of eye movements evoked by stimulating either the mesial cortex or the presylvian region. The results for one cat are shown in Table 1. For this animal, the latencies can be grouped about two averages, 44 and 64 msec. Within the lateral wall of the presylvian sulcus (called the 'lateral' area, vertical cross-hatching in Fig. 4), the average latency for the upward vector components in cat 1 was 66.3 msec (see Table 1, row 1). In this same area the average latency of the downward components was 41.4 msec. The probability that these means were drawn from the same population is much less than 1/1000. In the same cortical area the latency of the ipsiversive component was also significantly larger than that of the component directed towards the contralateral side (row 2 of Table 1). Consequently, oblique eye movements directed ipsilateral-down or contralateral-up, had components with unequal latencies. For instance, an eye movement ipsilateral-down had a long latency ipsilateral component, and a short latency down component.

In both the mesial cortex (except the anterior dorso-medial corner in section A of Fig. 1) and the medial wall of the presylvian sulcus, all directional components had latencies close to 45 msec. Both these cortical areas are grouped under the name 'medial' area and are indicated by horizontal cross-hatching in Fig. 4. For example, the latencies of the up and contralateral components were 48.0 msec and 43.7 msec, respectively (Table 1, row 3).

Table 1, row 5, also shows that the mean latencies of the up components in the 'medial' area, and the down components in the 'lateral' area, were not significantly different; whereas row 6 shows that a contralateral component evoked in the 'medial' area had a significantly shorter latency

than an ipsilateral vector elicited in the lateral wall of the presylvian sulcus.

An exception to the short latencies associated with components in mesial cortex are the long latencies found in the most anterior dorsomedial corner of this region (Fig. 4A, stippled area). For example, the upward directed eye movements there had similar latencies to the ones found lateral to the presylvian sulcus (Table 1, compare rows 1, 2 and 4). The similar, long latencies (and the presence of ipsiversive directional eye movements) in both the lateral presylvian area, and in the anterior dorsomedial area, suggest that these regions may be similar functionally ('lateral' area), and may be linked by a strip of frontal cortex. A similar strip may also unite the two regions comprising the 'medial' area. The relationship between these zones and cytoarchitectural subdivisions will be considered in the discussion.

Evoked neck muscle activity

Figs. 5A and 5B illustrate the typical time relations between single evoked neck EMG responses in the biventer cervicis muscle, summated EMG's for 40 trials, and associated eye movements.

On the left of Fig. 5A, the EMG data were derived from the lateral wall of the presylvian sulcus (solid pointer) and were associated with eye movements directed mainly upwards. Similar results were obtained from the anterior dorsomedial wall of the hemisphere, and this is indicated by the dashed pointer. The EMG consists of a double burst of activity with a latency to the first peak of some 40-50 msec. It is noteworthy that the first synchronous burst of EMG activity preceded the evoked eye movements by some 25-30 msec. Such timing is similar to that seen in monkey during coordinated

head and eye movements towards unpredictably located targets[7]. The EMG activity evoked at this point and all others seemed independent of the initial position of the eye in the orbit. The EMG trace in Fig. 5A shows also that the first evoked burst of activity was preceded by a short suppressive period. Careful scrutiny of the vertical eye movement component (V) does indeed reveal a small initial downward movement typical of frequent composite eye movements evoked in this cortical area.

As the stimulating electrode progressed nearly parallel to the grey matter of the lateral wall of the presylvian sulcus, the evoked eye movements reversed direction. An analogous reversal occurred in the EMG response. This is shown in the data to the right of the coronal brain section of Fig. 5A. The peak of activity at 45 msec, associated with an upward movement, was totally suppressed and replaced by a trough. This suggests a coordinated attempt to lower both head and eyes. The significance of the second peak of activity at 80 msec in the EMG histograms of Fig. 5A is unclear (but could reflect the influence of indirect pathways; the activity of feedback loops concerned with the abnormal restraint imposed on the head; or the phenomenon of spindling).

Fig. 5B shows, on the left, EMG activity evoked in mesial cortex in conjunction with oblique contralateral eye movements. The shape of the EMG histogram is similar to that on the left of Fig. 5A, but the latencies of the peaks are shorter. This is consistent with the short latency (some 45 msec) eye movements elicited from this cortical area (Table 1, row 3). Again, a burst of EMG activity precedes the eye movement, in this case by some 15 msec.

The summated EMG activities, related to the up and down components of goal-directed or centering movements evoked by stimulation of the lateral

area, are shown in the right histograms of Fig. 5B. This EMG activity consisted of a stereotyped burst whose characteristics seemed independent of the direction of the evoked eye movements, implying a direction of intended head movement unrelated to eye movement direction. A similar result has been seen during stimulation of the caudal portion of the superior colliculus in cats with restrained heads[27].

Influence of stimulus parameters

The dependence of the evoked eye movements on changes in the stimulus parameters were generally similar to those reported by Schlag and Schlag-Rey[43]. The threshold current was defined as that necessary to evoke eye movements in 25% of the trials. In all areas studied this threshold was close to 50 μA. Even if the current exceeded threshold by a factor of 6, the number of evoked eye movements rarely exceeded 80% of the number of applied stimuli. For a given current, doubling or halving the pulse width, train length, or pulse frequency had little or no effect on amplitude, direction, latency or threshold of an evoked eye movement. With large currents (300 μA) and with long trains (200 msec) the saccade amplitudes were somewhat increased, but this was thought to be due to arousal effects, because stimulation at such intensities was frequently accompanied by dilatation of the pupils. Indeed, the most influential factor affecting saccade characteristics was the animal's state of alertness: eye movements could not be elicited reliably in a drowsy animal.

The current necessary for evoking EMG activity in the biventer cervicis muscle depended on the cortical area stimulated. In the 'medial' area the threshold was about similar to that necessary for evoking eye movements. In the 'lateral' area the threshold was lower: the standard train with a 10 μA current was frequently sufficient, and with a 50 μA current only a single pulse was necessary to elicit a strong and reliable change in EMG activity

DISCUSSION

Four major findings have emerged from this study: (i) focal stimulation within the cat frontal lobe evokes eye movements whose directions are topographically organized; (ii) on the basis of directions and latencies of evoked eye movements, and thresholds for evoking neck EMG activity, the frontal 'oculomotor' area can be divided into two sub-regions; (iii) the evoked eye movements are frequently preceded by neck muscle activation, which, within the limits imposed by the present techniques, appears compatible with a coordinated eye-head orienting response, and (iv) the eye movements evoked from the medial sub-region resemble those evoked from the FEF of monkey.

Location of excitable cortex

The present experimental results are in excellent agreement with those of Hassler[29] and Schlag and Schlag-Rey[43] regarding the observation that eye and head movements can be elicited from the walls and fundus of the presylvian sulcus. There is less agreement, however, regarding the location and extent of excitable cortex in the more medial regions. Hassler[29] showed that movements of head and eyes can be elicited from a major portion of the lower lip of the cruciate sulcus, including the medial anterior sigmoid gyrus. Schlag and Schlag-Rey[43], on the other hand, obtained no responses from this region. The latter authors did, however, elicit eye movements from the wall of the mesial hemisphere in the neighbourhood of, and dorsal to, the sulcus genualis. The present study is in good agreement with Schlag and Schlag-Rey[43] regarding the existence of a region of responsive cortex in the mesial wall extending approximately 1 mm anterior to 2 mm posterior to the lip of the cruciate sulcus (Fig. 1A-C). However, the present findings indicate that excitable mesial

cortex also extends onto a portion of the lower lip of the cruciate sulcus (Fig. 1D-E), in partial agreement with Hassler's responsive area[29].

Characteristics of evoked eye movements

Eye movements evoked from cat frontal lobe were rapid and saccade-like, but were consistently faster than spontaneous saccades made by alert animals. Crommelinck and Roucoux[13] have shown that the degree of arousal of a cat has an important effect on the maximum velocity of the spontaneous saccades; a strongly aroused cat, injected with amphetamines, can produce saccades which are twice as fast as those made by a drowsy animal. Therefore, it is probable that the ocular movements evoked in the present experiments correspond to true saccades generated by a highly aroused animal.

In the study by Schlag and Schlag-Rey[43] with encéphale isolé preparations, stimulation within cat frontal lobe evoked primarily centering eye movements. This finding was not confirmed in the present experiments where centering movements were confined to the 'lateral' area (Figs. 1 and 4). The discrepancy could have been due to different arousal levels between preparations[4,51]. With awake and alert animals centering movements were restricted to the 'lateral' area, whereas the other responsive cortical points yielded eye movements whose directions and amplitudes were independent of the position of the eye in the orbit. The direction of such non-centering eye movements depended on the site being stimulated, with a discrete and orderly representation of directions existing within the cortex (Fig. 1). There was no corresponding orderly and systematic variation in amplitude. This is in contrast to the 'foveation' type of eye movements evoked by stimulating the superior colliculus[11,39,42] where both

amplitude and direction depend systematically on the site being stimulated. This difference between the results of sub-cortical and cortical stimulation suggests that eye movements evoked from the 'medial' area are not referred to a retinotopic 'map'.

The agreement between this study and that of Schlag and Schlag-Rey[43], regarding eye movements, was best for cortex along the mesial wall of the hemisphere. In both studies, eye movements with a strong horizontal component were evoked. However, the distribution of evoked eye movement directions in the present study was in best overall agreement with the work of Hassler[29]. Both latter studies showed: (i) contraversive upward, and pure upward movements from the mesial cortex and its extension onto the lower lip of the cruciate sulcus (Fig. 1D and E); (ii) upward movements from the dorso-medial wall of the presylvian sulcus (Fig. 1C); and (iii) ipsiversive movements from the anterior lateral wall of the presylvian sulcus (Fig. 1A and B).

Eye-head coordination

At all sites where eye movements could be evoked, the change in EMG activity evoked in biventer cervicis neck muscle preceded the eye movement. This was reminiscent of the observations by Bizzi et al.[7], for monkeys orienting towards targets appearing unexpectedly in their visual field. While the present results were obtained in cats whose heads were restrained, Hassler[29] has described coordinated eye and head movements in response to stimulation of the same frontal areas in alert unrestrained cats. In the present study, the EMG responses in the 'lateral' area seemed independent of the cat's arousal level and were present even for stimulus currents markedly below those necessary for evoking eye movements. This, in conjunction with the presence in the lateral wall of the presylvian sulcus of cells which discharge before neck muscle activity[26], suggests that this responsive

frontal area may be primarily involved in the control of head movement. If this be the case, evoked eye movements might depend on head position. The present technique did not permit a direct investigation of this problem. It was, however, verified that the eye movement characteristics did not depend on the level of EMG activity in the biventer cervicis muscle.

Functional subdivisions

The boundaries of the 'medial' and 'lateral' areas (Fig. 4) are in striking agreement with those delineated by direct fiber projections from the cat frontal cortex to the internal medullary lamina of the thalamus. Orem and Schlag[36] have shown that the lateral and dorsal walls of the presylvian sulcus (vertically cross-hatched in Fig. 4), and the anterior dorsomedial wall of the hemisphere (stippled area in Fig. 4) project directly to the nucleus centralis lateralis (CL). Schlag and his collaborators also stimulated the thalamus[44] in search of oculomotor responses and found that eye movements could be elicited only from CL, and that such responses did not depend on the integrity of frontal cortex. These results, in conjunction with the present ones, suggest that the long latency eye movements elicited from the 'lateral' area are mediated via a thalamic CL pathway. However, a contradiction exists: contraversive and primarily horizontal movements were evoked by directly stimulating CL[44], whereas in the present study stimulation of the 'lateral' cortical area evoked either centering movements or ipsiversive movements with strong upward components.

In contrast to the 'lateral' area, the mesial wall of the hemisphere, dorsal to sulcus genualis, projects directly to the nucleus medialis dorsalis (MD; 36). Stimulation of MD, however, does not elicit eye movements[44]. The question therefore arises as to those pathways that mediate short

latency eye movements elicited from the 'medial' area. The routes from the frontal cortex to oculomotor neurons, through which eye movements are evoked, are necessarily polysynaptic[40]. Impulses originating in the 'medial' area may reach oculomotor nuclei via the cerebral peduncles[49], and there is some evidence that the superior colliculus is implicated in this pathway.

Frontal eye field and superior colliculus

The FEF of monkey, and probably the 'medial' area of the frontal oculomotor region of cat, project to the superior colliculus (SC; see refs. 2,24,25,33a). Since the SC has been implicated in orienting responses[42,48], it has been natural to suspect that it plays an important role in mediating eye movements elicited by frontal lobe stimulation. In monkey, this notion has been rejected because SC ablation may not abolish eye movements evoked by FEF stimulation[41]; and because the shortest latency from the start of a suprathreshold FEF stimulus to that of an evoked saccade was 15 msec[40], compared to 20 msec for SC stimulation[39].

The situation may be different in cat. Indeed, present results show that eye movements evoked by stimulating the medial areas (horizontally cross-hatched in Fig. 4), had a 45 msec latency, whereas for near identical stimuli, SC stimulation resulted in 20-30 msec latencies[11]. It therefore seems possible that, unlike monkey, the SC of cat could be mediating eye movements elicited by stimulation of portions of the frontal lobe. Consistent with this hypothesis is the fact that cells responding to stimulation of the medial areas within frontal lobe of cat have been recorded in the intermediate and deep layers of the SC, and their response latencies varied between 7 and 30 msec[24,25]. Furthermore, in the 'medial' area, cells

have been described that respond in association with, and prior to, visually triggered eye movements[26].

Cytoarchitectural areas

The cytoarchitectural studies of cat frontal lobe[28,30,45,52] show little agreement regarding the location of specific sub-divisions. This is particularly true for the general area surrounding both sides of the presylvian sulcus.

The subdivisions of the mesial cortex, and its extension under the lip of the cruciate sulcus, are less controversial: all relevant studies place areas 6 and 4 within this territory. Below the lip of the cruciate sulcus, Hassler and Muhs-Clement's areas 6aβ and 6aδ[29,30] correspond to area 6 of Winkler and Potter[52], and to the more caudal cortex from which eye movements and neck muscle activity have been evoked in the present study (Figs. 1D,E and 4D). The observation that orienting responses of eye, head, and trunk can be elicited from area 6 is not unique to cat but has also been shown for monkey[50].

There is less agreement between the rostral extent of area 6 (or 6aβ), and the rostral extent of responsive mesial cortex found in the present study. Indeed, in the present experiments, no eye movements could be elicited from the most rostral portion of the lower lip of the cruciate sulcus (Fig. 1B). The eye movements elicited from the most anterior dorsomedial corner of the hemisphere (Fig. 4, stippled area) were of a different type, and this region was considered part of the 'lateral' area.

The location of specific cytoarchitectural subdivisions can vary considerably between individual animals[30,37] and may account for the difficulties in relating functional properties to cytoarchitectural areas. Nevertheless, within the limits of this variability, the region of responsive

mesial cortex represented by horizontal cross-hatching in Fig. 4 can be considered to be coextensive with at least a portion of area 6.

The region surrounding the presylvian sulcus has been named area 6 by Gurewitsch and Chatschaturian[28], area 10 by Winkler and Potter[52], and area 8 by Scollo-Lavizzari[45]. Schlag and Schlag-Rey[43] have suggested that the presylvian area in cat is homologous with monkey FEF (Area 8). Their conclusion was largely influenced by the proximity of the presylvian region to the cortical motor representation of the face. Their view, however, may be an oversimplification.

The present results have shown that stimulation of both the mesial cortex and the medial wall of the presylvian sulcus ('medial' area, horizontal cross-hatching, Fig. 4) in cat elicits activation of the contralateral neck muscle, and largely contralaterally directed eye movements, whose latencies are shorter than those obtained from the lateral presylvian area. Short latencies, as well as contralaterally directed eye movements, are consistent with results obtained by stimulation of the FEF in monkey[40].

These observations, together with the demonstration of (a) projections in cat from the 'medial' area to MD and possibly SC[24,25,36]; and (b) analogous projections in monkey from FEF to MD and SC[2,33a], suggest that the entire 'medial' oculomotor area (Fig. 4, horizontal cross-hatching) in cat is homologous with monkey FEF. However, this conclusion, derived from stimulation studies, seems incomplete, as unit recording has revealed cells in both the 'lateral' and the 'medial' areas, with properties resembling those recorded from monkey FEF[26].

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TABLE 1

	CORTICAL AREA*	COMPONENT OF EYE MOVEMENT VECTOR	MEAN LATENCY	STANDARD DEVIATION	NUMBER OF SAMPLES	't'	P
Cat 1	1. LATERAL	Up Down	66.3 41.4	9.0 18.0	65	7.4	<0.001
	2. LATERAL	Ipsilateral Contralateral	64.4 42.9	16.8 27.6	80	4.2	<0.001
	3. MEDIAL	Up Contralateral	48.0 43.7	13.1 16.1	178	2.0	0.05
	4. ANT. DORSO-MED.	Up	60.0	10.4	20	-	-
	5. MEDIAL LATERAL	Up Down	48.0 41.4	13.1 18.0	124	2.0	0.05
	6. MEDIAL LATERAL	Contralateral Ipsilateral	43.7 64.4	16.1 16.8	137	7.4	<0.001

* LATERAL refers to the lateral portion of the presylvian area, identified by vertical cross-hatching in Fig. 4. MEDIAL refers collectively to the mesial wall of the hemisphere, and the medial part of the presylvian area, shown by horizontal cross-hatching in Fig. 4. ANT. DORSO-MED. refers to the corner of medial hemisphere shown stippled in Fig. 4.

TABLE 1

Fig. 1 (Fig. 6-1)

Coronal sections through the cat's right frontal lobe, indicating the types of eye movements obtained in response to electrical stimulation at given sites. Section A is 0.4 mm rostral, while sections B-E are, respectively, 0.8, 2.4, 3.2 and 3.9 mm caudal to the dorsal extension of the cruciate sulcus. Areas enclosed within interrupted borderlines are regions from which eye movements have previously been evoked[43]. The angular orientation of a single arrow indicates the direction, with respect to the animal's midline, of eye movements evoked by stimulation at arrow origin (left is contralateral). The length of each arrow is proportional to the mean saccade length (scale in lower right corner = 5 deg). Arrow heads converging upon a circle indicate centering eye movements. Crosses denote sites where stimulation evoked saccades having no consistent direction. Plain circles indicate points where stimulation had no effect. The bent arrow in A indicates composite saccades where eyes responded with an uninterrupted movement first in one, then in the other direction. Data derived from three animals. CO, coronal sulcus; CR, cruciate sulcus; PR, presylvian sulcus.

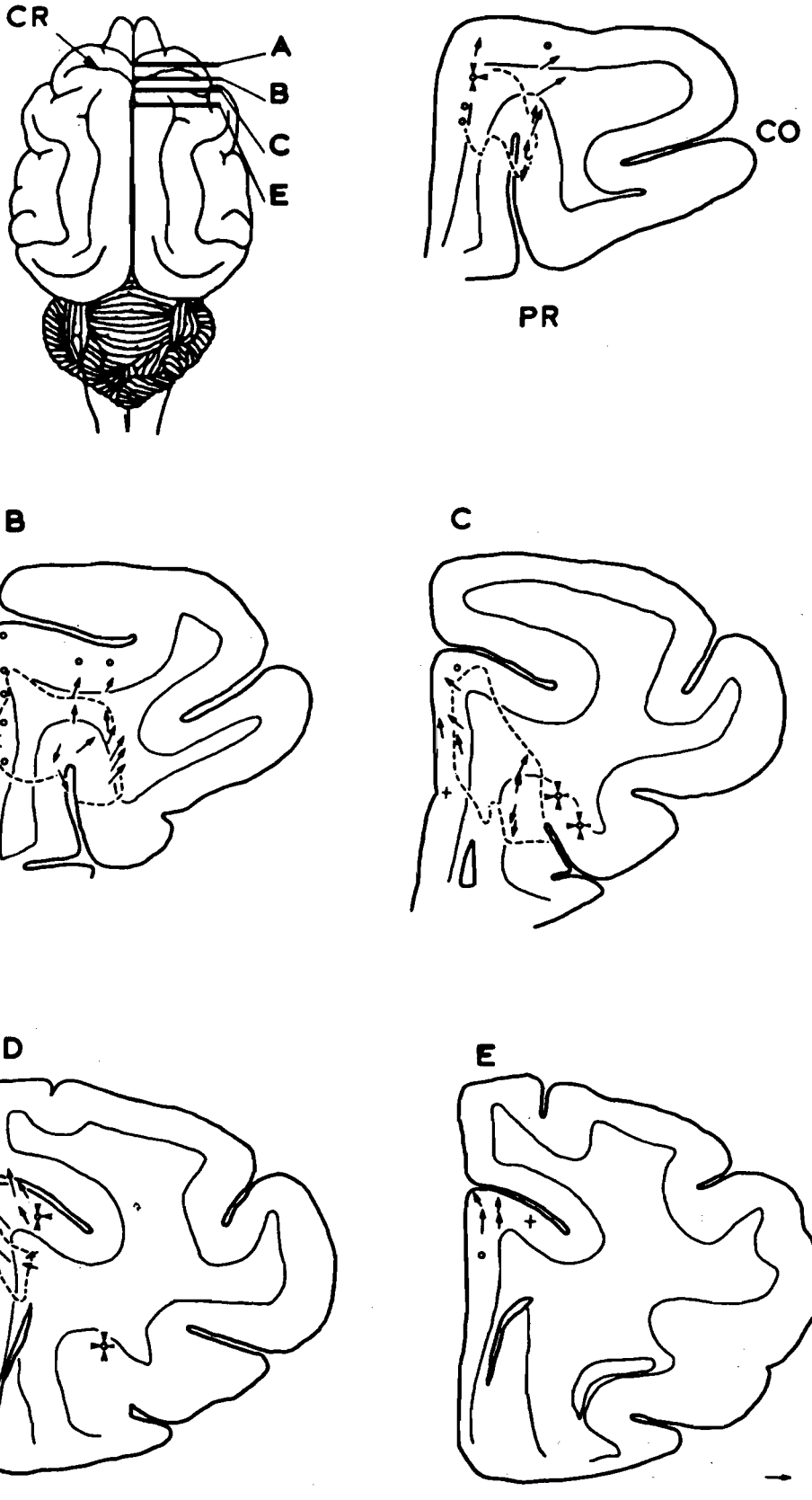

CR
A
B
C
E
A
CO
PR
B
CR
C
D
E

Fig. 2 (Fig. 6-2)

Projection of saccadic eye movements upon polar diagrams of the visual field. The intersections of horizontal and vertical coordinates indicate the cat's central gaze position (see Methods). Circles indicate the starting points, crosses the end points of saccades. Left in diagrams is contralateral. Stimulating currents: open circles, 50-100 μA; filled circles, 300 μA. A: contraversive saccades, obtained by stimulating the mesial wall of the hemisphere, (Fig. 1C). B: centering saccades, obtained by stimulating the lateral wall of the presylvian sulcus (Fig. 1C).

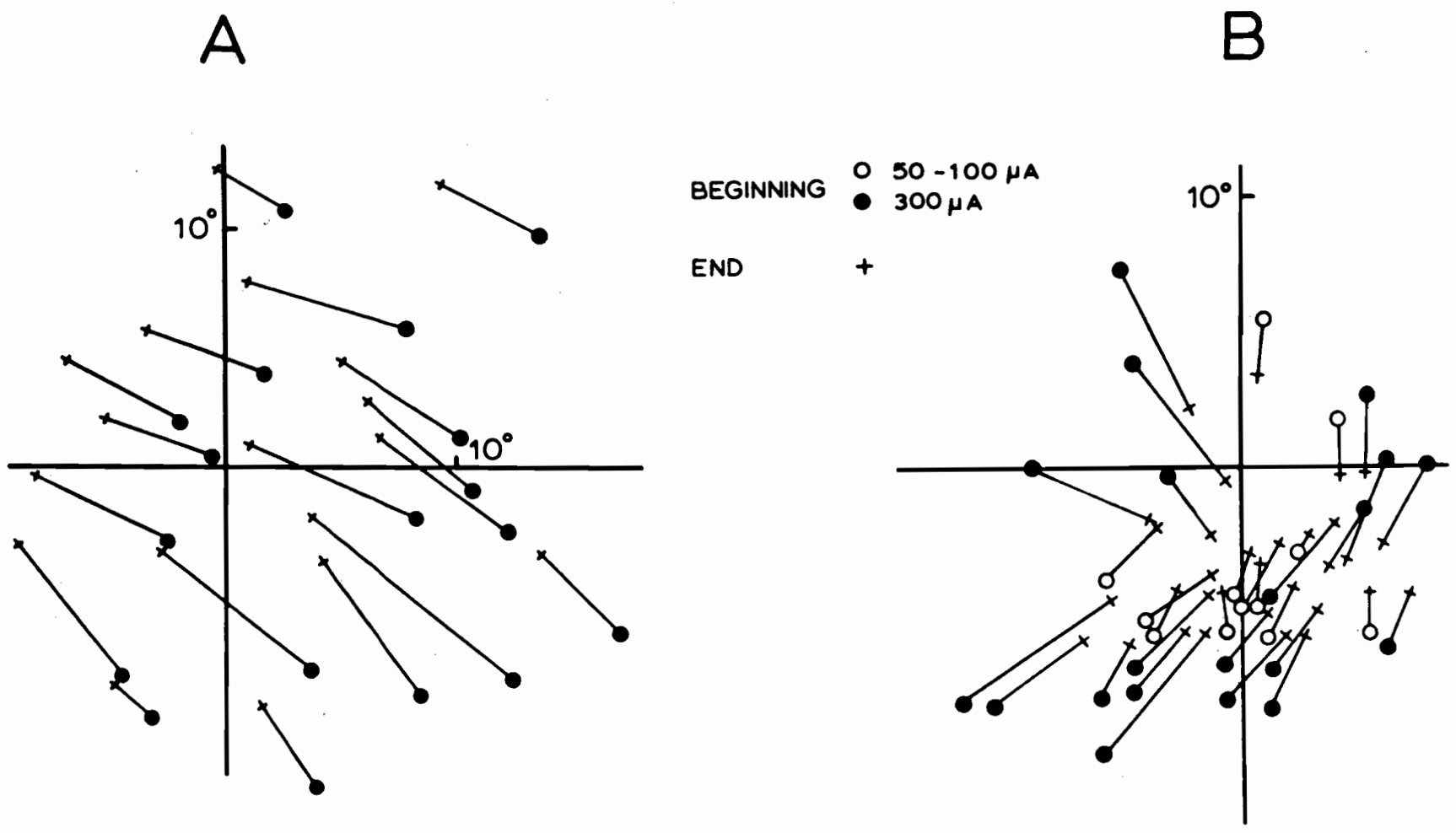

A
10°
10°
BEGINNING
50 - 100 µA
300 µA
END
B
10°

Fig. 3 (Fig. 6-3)

Correlation of the velocity with the amplitude of cat saccadic eye movements. Note that saccades evoked by cortical stimulation (open circles, r = 0.87) are faster than normal 'spontaneous' saccades (filled circles, r = 0.84). This is also illustrated by two examples of, respectively, spontaneous and evoked saccades. Time bars indicate stimulus of 60 msec duration. Common amplitude scale: 10^{o}.

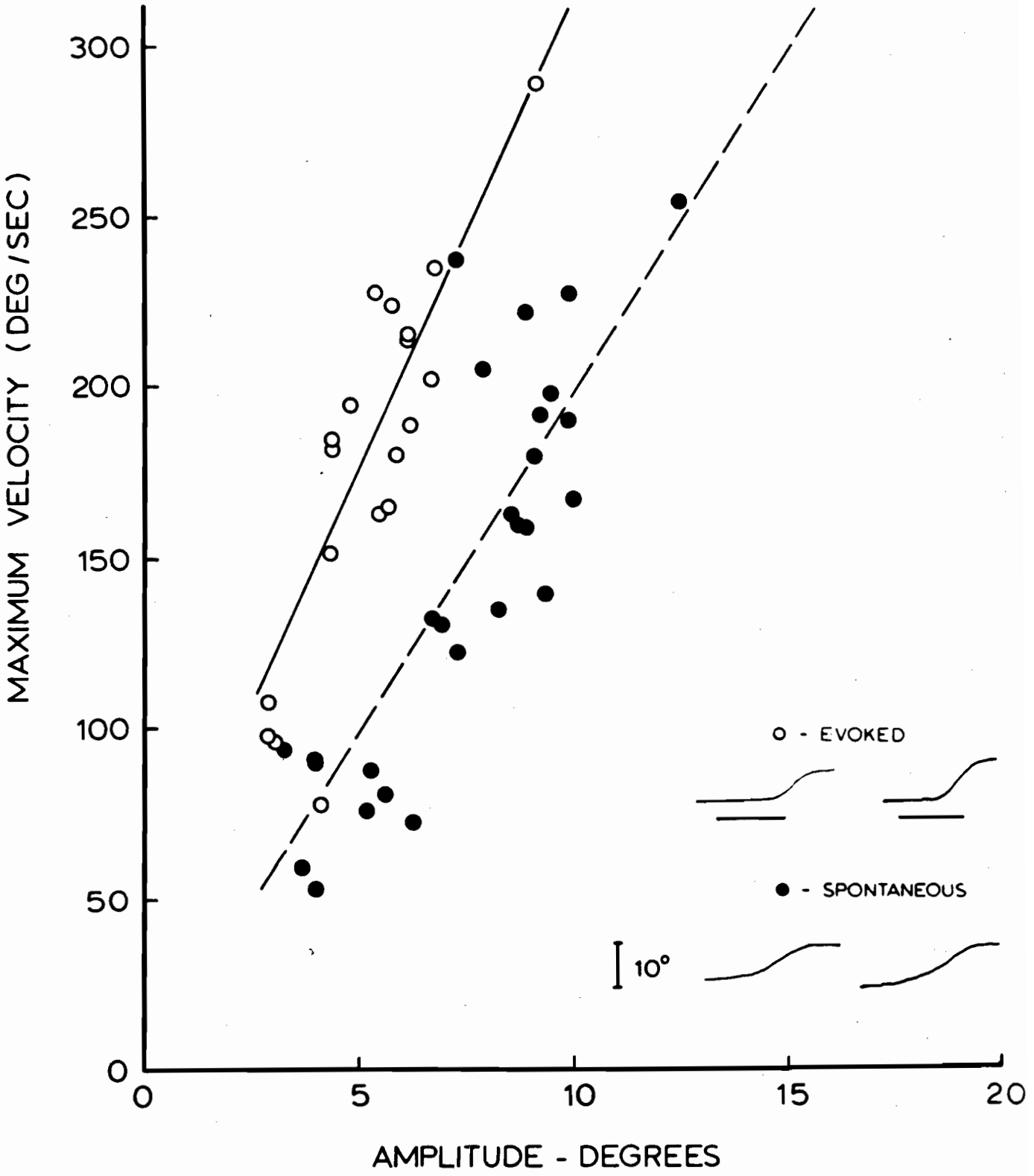

MAXIMUM VELOCITY (DEG/SEC)
300
250
200
150
100
50
0
0
5
10
15
20
AMPLITUDE - DEGREES
O - EVOKED
● - SPONTANEOUS
10°

Fig. 4 (Fig. 6-4)

Subdivision of cat frontal 'oculomotor' region according to the latencies of directional components of evoked eye movements. Vertical cross-hatching: long latencies for upward and ipsiversive components, short latencies for downward and contraversive components. Stippled area: long latencies for upward components; latencies of downward, ipsiversive and contraversive components are uncertain. Horizontal cross-hatching: short latencies for all evoked directional components. Sections as in Fig. 1.

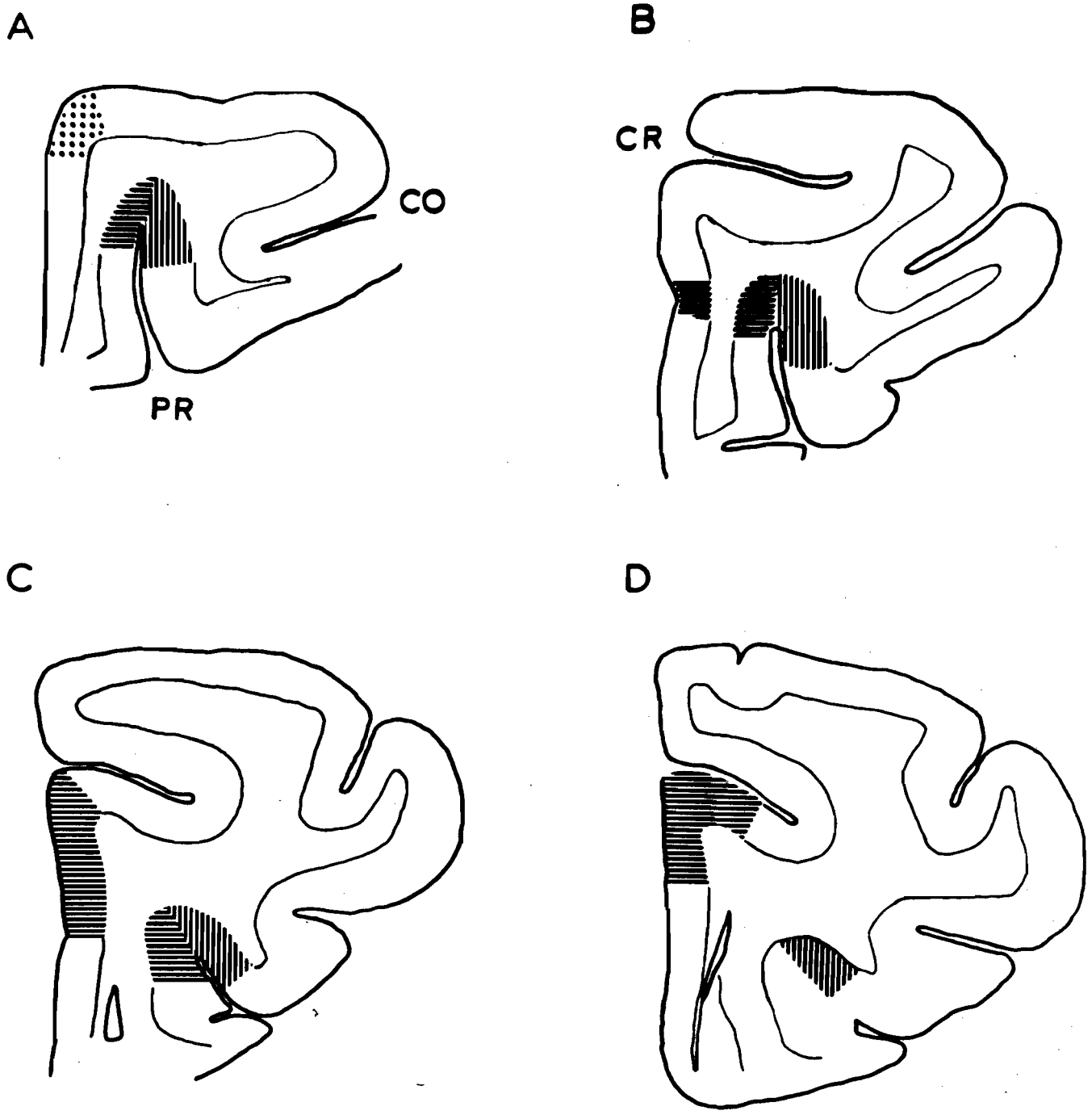
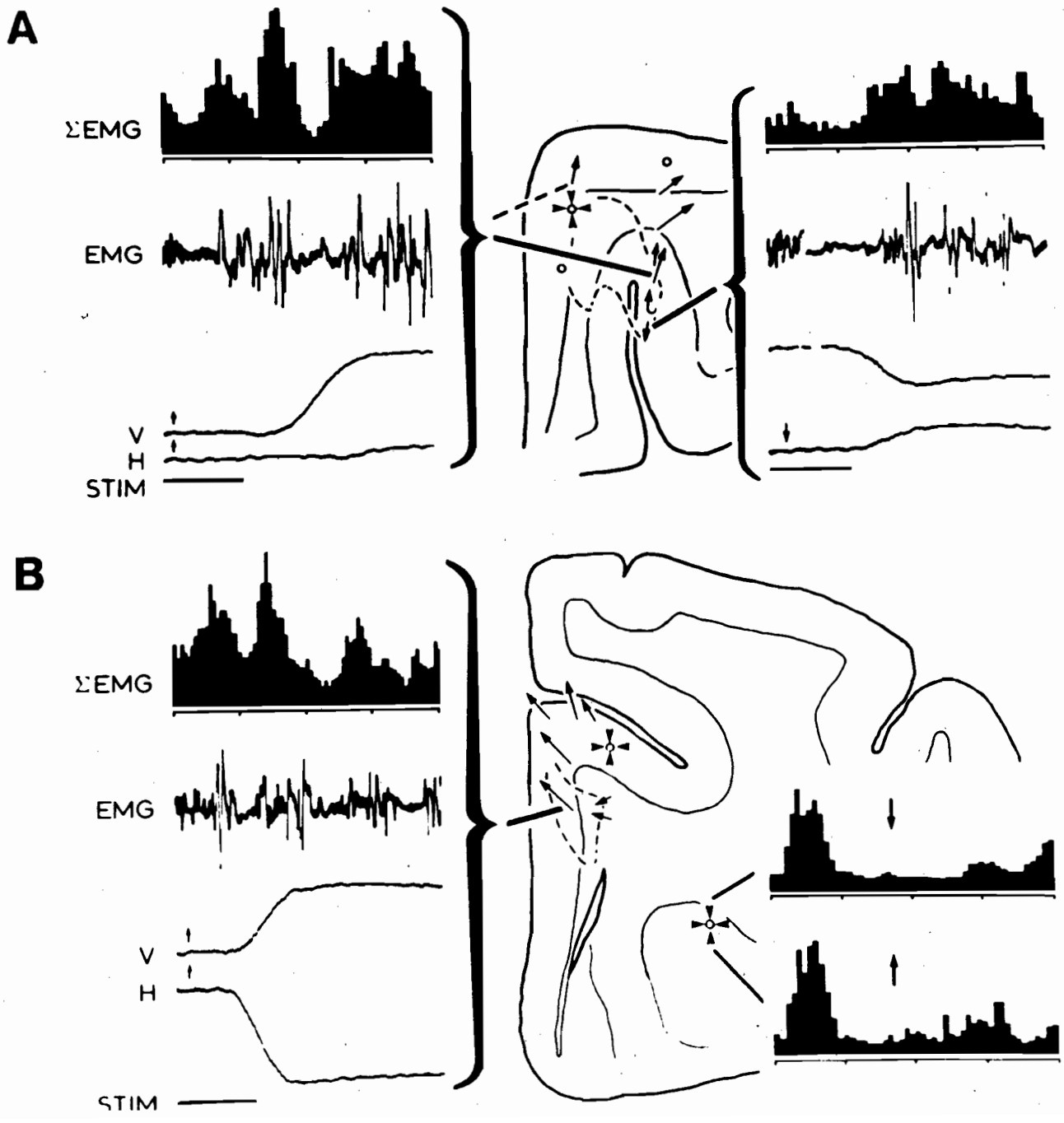

A
CO
PR
B
CR
C
D

Fig. 5 (Fig. 6-5)

Time relations between evoked neck muscle responses and associated eye movements evoked from specific cortical points. Σ EMG: average response histogram (ARH). 40 summated biventer cervicis neck muscle responses. Time marks: 50 msec. EMG: single representative evoked response from neck muscle (retouched). V,H: vertical and horizontal eye movements, with arrows indicating eye movements up and to the right, respectively. STIM: duration of cortical stimulus, 60 msec. A: left panel shows data derived from the lateral wall of the presylvian sulcus (solid pointer). Initial burst of neck EMG precedes upward saccade by some 25-30 msec. Note also brief suppression of activity preceding this first burst, anticipatory of the small initial downward component in the V trace. The results obtained from the dorso-medial cortex (dashed pointer) were similar. Right panel shows suppression of EMG activity precedes downward eye movement by some 30 msec. B: left panel shows data derived from stimulation of mesial cortex. Short latency muscle activity associated with short latency eye movement. The initial EMG burst, which has a latency of some 35 msec, precedes the onset of the eye movement by some 10-15 msec. Right panel shows arrows associated with the EMG histograms indicating the directions of goal-directed eye movements with which each respective histogram is associated. Note the close similarity between these two histograms, despite opposing directions of eye movements.


A
ΣEMG
EMG
V
H
STIM
B
ΣEMG
EMG
V
H
STIM

CHAPTER 7

FRONTAL 'OCULOMOTOR' AREA IN ALERT CAT: II. UNIT DISCHARGES ASSOCIATED WITH EYE MOVEMENTS AND NECK MUSCLE ACTIVITY

Status: Brain Research 149 (1978) 313-327

Authors: Guitton, D. and Mandl, G.

SUMMARY

(1) Unit activity in frontal 'oculomotor' cortex was recorded extracellularly from sites where subsequent electrical stimulation, using threshold current (50 μA), could elicit both eye movements and simultaneous neck EMG activity.

(2) Of 103 cells, 19% were related to either eye movements or neck EMG activity. Cells could be grouped into three categories: (a) Directional (D) cells (31%) discharged before and during saccadic eye movements, whenever the eyes followed a target in one specific direction. Spontaneous saccades, or vestibularly driven nystagmus, in either the light or dark, elicited no responses. (b) Conditionally directional (CD) cells (43%) discharged following (i) tracking saccades; (ii) spontaneous saccades and (iii) the quick phase of nystagmus, in all directions. There usually was a slight discharge preference for one given direction, and this preference was enhanced whenever visual tracking was restricted to the preferred direction. One-third of CD cells responded to stimulation of the contralateral biventer cervicis neck muscle (min lat. 20 msec). (c) Neck EMG (N) cells (26%) discharged in association with, and preceding changes in neck muscle activity. These cells also responded to stimulation of the contralateral biventer cervicis muscle (min lat. 10 msec).

(3) For points in the lateral 'oculomotor' region (as defined by stimulation: see ref. 17), the directions of evoked saccades, and the directions of spontaneous saccades associated with unit discharges, were similar. In the medial region[17], the directions of evoked saccades were roughly opposite to the directions of spontaneous eye movements favoured by unit discharges.

FEF UNIT DISCHARGES ASSOCIATED WITH EYE MOVEMENTS AND NECK MUSCLE ACTIVITY

INTRODUCTION

The human and simian frontal eye field (FEF) has been classically considered to be the cortical motor area responsible for initiating voluntary eye movements. The proximity of the FEF to motor cortex; the contribution of its efferent fibres to the pyramidal tract; and observations following stimulation [1,5,7,20,21,29,34,40], were taken as evidence in support of this view. Many of the initial deficits[23,24], observed after ablation of the FEF, have also lent credence to this hypothesis. However, these initial deficits gradually disappear, and the remaining ones suggest that the function of the FEF is other than motor[25,26,27]. Among the most important long-lasting ablation deficits has been the tendency for perseverative fixation and tracking of visual targets[20,23,40]. Similar clinical observations led Holmes[20] some forty years ago to suggest that the FEF was necessary for the purposeful scanning of the environment, where attention, discrimination and recognition are necessary to select and to fixate relevant visual targets. This view has received some support from more recent ablation experiments in monkeys, which showed a long-lasting reduction in their ability for unpractised visual search[27,28].

In the FEF of monkey, single cells whose activities are associated with eye movements were found to discharge after the start of saccades[2,3,30]. This finding has finally discredited the hypothesis that the primate FEF is an oculomotor area, but has not offered further evidence to elucidate the still obscure functional significance of this cortical region.

In cat, stimulation of frontal cortex also elicits eye movements[17,18,37] and ablation of this excitable region yields behavioural deficits similar to those reported for monkey[22,36]. In the preceding paper[17], a quantitative study has been made of the latencies and directions of eye movements evoked by focal stimulation within the frontal oculomotor region of cat. The results indicated the presence of two functionally related sub-regions, of which the 'medial' seemed homologous with monkey FEF. In the experiments to be described in this paper, unit activity was monitored within the same frontal lobe regions of untrained, alert cats, while the animals performed visual tasks, some of which resembled those affected by FEF lesions. The discharge characteristics of cortical units, and concurrent neck muscle activity, were monitored while the animals: (i) made spontaneous eye movements in both light and dark; (ii) attentively tracked targets moving either randomly or periodically within the visual field; and (iii) were rotated to induce vestibular nystagmus.

The results indicate the presence of directionally specific cells whose discharges favour specific directions of eye movements, and cells whose directional specificity is enhanced when visual tracking is restricted to back and forth motion along a line of a given orientation. Cells whose activity precedes, or coincides with, neck muscle activity were also found. The results further corroborate the existence of two separate areas within the cat frontal 'oculomotor' region[17], but suggest that both the 'medial' and 'lateral' areas of cat contain functional components which, in the monkey, are placed within the confines of the FEF.

METHODS

A detailed description of the experimental procedure, including the animal preparation, the methods for the recording of eye movements, of single unit discharges, and of the neck muscle EMG, have been given elsewhere [17].

Briefly, cats were first trained to remain relatively immobile for periods of some 1-2h. Following this initial accommodation period, each animal was fitted with a surgically implanted scleral eye coil which provided records of eye position [12]; an EMG electrode placed within the left biventer cervicis neck muscle; and an acrylic head implant. A steel well providing access to the right frontal lobe, and threaded brackets designed to anchor the head to a stereotaxic frame, were embedded in the ac rylic implant.

The cat and the field coils of the eye position recording device [17] were mounted on a horizontally rotating table. Records were taken in the light, in the dark, while the animal looked about spontaneously, while it tracked small rubber spiders or mice and during horizontal vestibularly induced nystagmus. Each visual target, mounted on a circular metallic base, was held and moved against a white smooth cardboard tangent screen (distance 50 cm) by means of a magnet, hand operated from the other side. Nystagmus was produced by rotating the table at about 0.7Hz, with a peak to peak amplitude of 30^{o}.

RESULTS

While testing unit responses during visual tracking, it was found that the untrained cats would not remain attentive to slowly moving targets. Recently, Evinger and Fuchs[11] have shown that for cat, the gain of smooth pursuit eye movements in response to sinusoidal target motion was down by 3 db at a peak velocity of 6 deg/sec. In the present experiments, the target velocity was always greater than 6 deg/sec, and consequently all tracking eye movements were saccadic in nature (Figs. 1 and 2).

One hundred and three cells were studied in sufficient detail to establish basic response categories. Responses that were clearly related to either eye movements or neck EMG activity were found in 19 cells (19%). Cell responses could be grouped into three categories: (i) Directional (D) cells (31%) responded with a burst discharge when the animal visually tracked a target moving in one specific direction; (ii) Conditionally directional (CD) cells (43%) discharged in association with spontaneous or tracking saccades and quick phases of nystagmus in all directions. There usually was a slight discharge preference for one direction, and whenever the animal tracked a periodically moving target in that direction the CD cells exhibited greatly enhanced directional specificity; (iii) Neck EMG (N) cells (26%) discharged in synchrony with, and preceding, a change in neck muscle activity.

Directional (D) cells

Fig. 1 shows the discharge pattern of a D cell recorded while the animal was tracking a target moving sinusoidally (hand approximated) in a predominantly vertical direction. The amplitude of movement was about 10^{o}, with a maximum velocity of about 20^{o}/sec.

The unit responded well in association with eye (and target) movements directed generally upwards. Discharges always preceded a step-like sequence of vertical saccades, but there was considerable variability in the response pattern. In some cases the frequency of the initial burst was high (saccades 1-2, 17-18, 21-22); in others, it was low (saccades 6-7, 10-11, 13-14); and in others (not shown) the activity was entirely absent. No correlation could be established between the variation in response and differences in eye position or eye movement patterns. For example, there is little difference between saccade sequences 1-2-3 and 13-14-15, yet the associated unit discharge patterns are quite different.

D cells did not respond in association with EMG activity in the biventer cervicis neck muscle, spontaneous saccades, and vestibular nystagmus, in the light or dark. The characteristic discharge pattern of these cells became evident only when the animals were tracking a target moving in a specific direction.

Conditionally directional (CD) cells

Fig. 2A-E illustrate responses of a single CD cell during various eye movement manoeuvres. CD cells were characterized by 3 features: (1) A burst of activity, associated with a saccade or quick phase, always began after the initiation of the eye movement; (2) unit activity was not related to the amplitude of eye movements, and (3) the burst discharge became strongly associated with a favoured direction of saccadic eye movement when the animal was tracking a target that moved back and forth along a line having a specific angular orientation. For some CD cells, a slight directional preference during non-tracking eye movements was present; for other units no consistent relation between

burst activity and eye movements could be found during rapid eye movements other than tracking.

Fig. 2A was obtained when the animal was making spontaneous saccades in the dark. Analysis of this brief record, together with records obtained during extended time periods (up to 3 min.) showed that this particular unit discharged in synchrony with, and after the initiation of,nearly all saccades, regardless of their amplitude or direction. For example, strong bursts are associated with saccades 1-2, 2-3, 5-6, 7-8 and 9-10, and the vector plots show that the associated eye movements have different directions and amplitudes (note that saccades 4-5 and 6-7 are also accompanied by weak bursts).

The unit activity shown in Fig. 2A also correlates with the EMG activity in the biventer cervicis muscle. However, examination of subsequent sections of Fig. 2 reveals that the CD cell discharge correlates best with eye movements: for example in Fig. 2B a number of burst discharges and associated quick phases are unaccompanied by EMG activity, and in Figs. 2D and 2E there is tonic EMG activity that is not obviously reflected by the unit activity.

The CD cell also discharged in association with, and after, the initiation of the quick phases of vestibularly induced horizontal nystagmus, in both dark and the light (Figs. 2B and 2C, respectively). In these 2 figs., the directionally non-specific nature of this unit's activity is again illustrated: bursts are associated with rapid eye movements directed toward all quadrants of the visual field.

Fig. 2D was obtained while the animal was tracking a target that was moved about the visual field in a non-specific manner. In this case the relation between the unit activity and saccades is more difficult to

assess. Indeed, there are a number of bursts which appear to be spontaneous, but which could be associated with small (< 1^{o}) eye movements that are not readily discerned with the scale used here: for example, consider the ripple in the plateau regions 2 and 9 of the H trace. The unit also occasionally discharged after a saccade had just terminated. Examples of this are saccades 4-5, 5-6 and 8-9. This latter feature can also be observed occasionally during the spontaneous saccades in the dark (saccade 1-2 in fig. 2A), and during quick phases of nystagmus (Fig. 2B and C). Although more difficult to detect in the case of Fig. 2D, the directionally non-specific nature of this unit seems conserved: burst discharges are associated with up (saccade 1-2), down (saccade 2-3), left (saccade 10-11), and right (saccade 5-6) components.

The characteristic feature of CD cells became apparent only when the cat was tracking a periodically moving target. Under these conditions, cells developed a directional preference. This is shown in Fig. 2E, where the eye position traces, in conjunction with the vector plots, show that the cell responded optimally during an eye movement dominated by a left-right horizontal component (contralateral to ipsilateral). The transition from a CD cell's directionally non-specific to a directionally specific firing pattern is shown in Fig. 3. This unit is the same as that shown in Fig. 2. On the extreme left of the traces, the target began to move from left to right in an oscillatory fashion in a near horizontal plane. It can be seen that the cell's directional characteristics were established at the beginning of the second cycle.

CD cell responses follow the onset of a saccade. (In this respect they are similar to unit responses in the FEF of monkey; 2, 3, 30). Records similar to those shown in Fig. 2 were obtained on an expanded

time scale and the relationship between burst latency and saccade onset was examined. Qualitatively, it appeared that burst latency increased with saccade duration, because the bursts frequently occurred during the deceleration phase. However, the bursts had initially a low frequency, and for this reason the precise timing of a burst was difficult to assess, particularly in the presence of spontaneous background activity. For example, some 100 saccades and associated unit burst discharges were analyzed, and of these only 25 bursts could be clearly defined. Consequently, the precise relationship between saccade duration and burst latency will not be examined here. For the identified bursts, the mean latency was 77 msec, with a standard deviation of 40 msec.

One-third of the CD cells responded to electrical stimulation of the contralateral biventer cervicis neck muscle. The earliest observed unit activity followed muscle stimulation with a latency of 20 msec. The CD unit discussed above, and shown in Figs. 2 and 3, responded with a single burst of activity that began some 40 msec after the initiation of the stimulus, and lasted some 100 msec.

Neck EMG (N) cells

The activity of these units was synchronized with, and preceded, changes in the EMG activity of the contralateral biventer cervicis muscle. No absolute correlation existed between unit discharges and muscle activity: bursts in the EMG sometimes occurred without concurrent unit discharges. Fig. 4A shows an example of an N cell recorded during vestibular nystagmus. The time relation between unit and EMG activity can be readily assessed by comparing the first and third traces. In the latter trace, the muscle activity is shown rectified and integrated (R-C integration), to facilitate the identification of changes in muscle

activity. By contrast, there is a lack of correlation between this unit's activity and eye movements, which can be verified by comparing the top trace with the eye position records (V and H).

All of the recorded N cells responded, in turn, to electrical stimulation of the biventer cervicis muscle (Fig. 4B). The earliest unit response followed stimulation by 10 msec, and the latency to the peak response varied between 15 and 30 msec. These latencies were therefore shorter than the latencies of similar responses recorded in CD cells.

Unit localization

An analysis of the latencies, and of the directions of eye movements elicited by stimulation of the frontal oculomotor region of cat, showed that this area consists of two sub-regions, referred to as the 'medial' and 'lateral' areas (see ref. 17, Fig. 4). The distribution of cell types between these two areas was as follows: 70% of D cells were found in the 'medial' area, whereas 90% of the CD cells, and all of the N cells, were found in the 'lateral' area.

Directions of evoked eye movements and unit directional specificity

All D, CD and N cells were recorded at sites where subsequent electrical stimulation elicited saccadic eye movements. In general, cells in the 'lateral' area preferred spontaneous eye movements in a direction similar to the evoked ones, whereas cells in the 'medial' area discharged in association with eye movements having a direction opposite to the direction of evoked saccades. This generalization is shown more specifically in Fig. 5.

Fig. 5A shows some data obtained from the 'lateral' area. The evoked eye movement vectors are indicated in boxes on the left, and

numerical values indicate the average directions obtained by stimulating cortical points marked with black dots[17]. For comparison, the series of encircled arrows on the right show the directions of spontaneous eye movements favoured by cells recorded just before focal stimulation was applied. The type of unit is indicated beside each circle. It was not always possible to specify precisely a unit's favoured direction. Thus, within a circle, the pair of arrows indicate a range of favoured directions, with the heavy arrows indicating the dominant vectors. It can be seen that there is good correspondence between the direction of evoked saccades, and the direction of spontaneous saccades associated with unit discharges. As the microelectrode progressed downward past a given point within the lateral bank of the presylvian sulcus, the direction of evoked eye movements reversed by nearly 180°. Stimulating at the reversal point evoked composite eye movements having first a downward, than an upward component[17]. A unit recorded at this transition point also had directional preferences quite unlike those recorded more dorsally: it discharged in association with both leftward and rightward horizontal movements, but favoured those carrying the eye from right to left.

Fig. 5B shows data obtained in the 'medial' area. Here, the direction of eye movement favoured by a given unit was roughly opposite to that evoked by focal stimulation.

DISCUSSION

In the studies on monkey FEF by Bizzi[2] and Bizzi and Schiller[3], the relative number of cells, whose discharges were related to eye movements, was very low and attained 10% and 4% respectively. In a later study by Mohler et al.[30], also on monkey FEF, the proportion was considerably higher: 22% of cells responded in association with saccadic eye movements, while 47% responded to visual stimulation. In the present experiments on cat, the proportion of eye movement related cells was intermediate between that found by the previous investigators in monkey. The most conspicuous feature to emerge from the present results was the existence of cells that discharged in association with specific directions of eye movements, and cells whose activity preceded and coincided with neck muscle activity.

Directional (D) cells

These cells did not discharge during either spontaneous eye movements or vestibularly induced nystagmus. The characteristic discharges occurred during a step-like sequence of saccades, as the cat tracked an object moving rapidly in a specific direction. The responses preceded the series of eye movements (Fig. 1) but were not strictly time locked to individual saccades. No correlation with either position or velocity of the eye could be found.

Units whose discharges precede, and accompany, only those eye movements that occur during visual tracking of an object of interest moving in a specific direction, resemble parietal lobe neurons in monkey[31]. It has been suggested that such cells might either be coding corollary discharges, or be implicated in the elaboration of command events associated with visually triggered volitional acts[31,32]. The

fact that D cells did not discharge during spontaneous saccades makes the coding of corollary discharges unlikely[31], and rules out a role for these cells as purely conventional upper motor neurons[10].

Some D cells were recorded in the caudal portion of area 6aβ (see ref. 19), the anterior portion of which receives visual input[4,13,14]. Visually driven units in area 6aβ respond to moving stimuli; they have large receptive fields which include the fovea and are not restricted to one hemifield[13,14]. Therefore, another possible function of D cells is sensory: they may respond to retinal error, or image slip, due to target motion relative to the momentarily immobile eye during inter-saccadic periods.

The 'medial' oculomotor area, where the predominant number of D cells was recorded, has been shown by stimulation studies to be most closely homologous to the FEF of monkey[17]. In the FEF of macaca mulatta, Mohler et al.[30] have reported a large percentage of cells that responded to visual stimuli but, like D cells, did not respond in association with spontaneous saccadic eye movements. Some of these cells also showed an enhanced response when the monkey was about to fixate the visual stimulus[42]. These observations may imply that extraretinal influences acted upon such units. The present experiments did not permit a distinction between the possible command, sensory or extra-retinal influences underlying the observed D cell discharges.

Conditionally directional (CD) cells

The response of CD cells always lagged an associated eye movement. These temporal characteristics are highly reminiscent of Bizzi's directional cells (Type I), and Mohler et al's pandirectional eye movement cells[30], both of which have been recorded in the FEF of

macaca mulatta. The present CD cells, recorded in cat frontal lobe, discharged in association with spontaneous eye movements made in all directions, but with some cells there was a favoured direction that was accompanied by a more pronounced discharge. In all cells a strong directional preference developed when target motion and concurrent visual tracking were restricted to back and forth motion along a favoured axis. For those cells that already had a preferred direction, that preference was greatly enhanced during periodic tracking along the favoured axis. It appeared that a cell's discharge pattern was indicative of the animal's increasing certainty that the target will continue its motion in the preferred direction. It is in this sense that the cell's discharge pattern seemed dependent upon a particular condition, or 'set'[31].

The majority of CD cells were encountered in the lateral wall of the presylvian sulcus ('lateral' area, ref. 17). In this zone, about one-third of these cells also responded to electrical stimulation of the contralateral biventer cervicis neck muscle. Converging, short latency (8 msec) projections to this cortical region from dorsal neck muscles and eye muscles have also been previously described[9]. Thus, it might be argued that the delayed activity of CD cells with respect to the onset of a saccade is due to inputs from eye muscle proprioceptors. Bizzi[2] has stated that, in the case of his Type I cells, this was unlikely because such cells did not discharge during either the slow phase of nystagmus, or during smooth pursuit movements. The presently observed long average latency between the onset of a saccade and the onset of a CD cell discharge (77 msec) also argues against a direct proprioceptive activation. It is interesting that this latency is larger than that reported in monkey[35].

Neck EMG (N) cells

N cells, which were found in the 'lateral' area, discharged only in association with voluntary neck muscle activity. They also responded with a latency of some 10 msec to neck muscle stimulation. This was some 10 msec faster than the response of CD cells to identical stimuli. In the 'lateral' area, the shortest response latency following direct stimulation of the contralateral biventer cervicis and splenius neck muscle nerves has been reported to be 8 msec[9]. The response of the N cells could be compatible with this time if account is taken of the present indirect method of stimulation (see Methods).

The discharge of N cells generally preceded a change in the activity in the biventer cervicis neck muscle. Consequently, these units appear analogous to the 'head movement' cells described by Bizzi and Schiller in monkey FEF (see ref. 3).

Fronto-thalamic relations

Schlag and his coworkers have suggested that, in the cat, eye movements elicited from the lateral bank of the presylvian sulcus ('lateral' area) are mediated via the internal medullary lamina (IML; refs. 33, 38). Schlag et al.[39] have described the properties of single units recorded in the cat IML in association with eye movements. That work, and the present unit study in the 'lateral' area, agree on the presence of directionally selective units in these two regions. Apart from this, the unit characteristics are quite different. First, the majority of units recorded by Schlag et al.[39] in IML responded before spontaneous saccadic eye movements which were not visually triggered. D cells that discharged before eye movements in the present study were always associated with visually triggered eye movements, while the CD cells discharged after the start of saccades.

Second, most of the units in the IML responded in association with saccades to the contralateral side, whereas the present work shows that units in the 'lateral' area prefer ipsilateral eye movements.

Cat frontal 'oculomotor' area and monkey FEF

Differences in the types of eye movements evoked by stimulation[17] have revealed that the frontal oculomotor area of cat can be subdivided into two areas: 'medial' and 'lateral'. This result has been corroborated by the present findings that distinctly different distributions of cell types exist in each region.

The short latency contralateral eye movements evoked from the 'medial' area[17], in conjunction with its projections to thalamus[33] and SC[15,16], have suggested that this area, rather than the 'lateral', is homologous to monkey FEF. The FEF has classically been regarded as an oculomotor area, but the discharge characteristics of units in the 'medial' area support the view[2] that this is not so: D cells discharged only in association with visually triggered eye movements, and CD cells discharged after the initiation of eye movements. Furthermore, the direction of eye movements evoked from the 'medial' area was opposite to that favoured by unit discharges there.

It has also been proposed that the FEF elaborates a corollary discharge[2,41]. It is unlikely that D cells in the 'medial' area are implicated in this process because D cells did not discharge in association with spontaneous saccades. The discharge characteristics of CD cells is more compatible with the requirements of a corollary discharge although their latency, following the onset of a saccade, appears too long (77 msec) for this proposed function[35].

The FEF has also been thought to play a role in the purposeful scanning of the environment[20,27,28]. D cells exhibited a property which may be compatible with this function: these neurones discharged only when the untrained animal attended to, and tracked, an object of interest.

The relation between the 'lateral' area and monkey FEF is less clear. In monkey, unlike cat, no goal-directed or centering movements have been evoked from the FEF, and only 0.2% of stimulated FEF sites have been reported to elicit ipsilateral saccades[34]. The low threshold for evoking neck muscle EMG and the observation that N cells, found only in this area, discharged prior to neck muscle activity, provides evidence that the 'lateral' area may act as a motor centre for head movements. Support for this view comes from the observation that the threshold for evoking eye and head movements was low[17], and that the direction of evoked eye movements and head movements (as inferred from neck muscle activity) was the same as that favoured by the D and CD cell discharges. Furthermore, both the N and CD cells receive proprioceptive inputs which may be necessary for the accurate performance of relevant motor acts requiring eye-head coordination[8,9].

In cat the possible range of eye movements is quite small compared to monkey, and the differentiation into two areas could be related to a species specific organization of head and eye movements during orienting responses. It should be noted that variations in the distribution of cell types[42] and corticocortical projections[6] in monkey FEF indicate that it too may not be a homogeneous zone.

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Fig. 1 (Fig. 7-1)

D cell activity recorded from 'medial' oculomotor area while the cat was tracking a small moving target. Target moving near-vertically back and froth in the visual field. AP: Unit activity. V: vertical eye movements, with horizontal bar indicating the central gaze position. Arrow indicates upward eye movement. H: horizontal eye movements, with bar indicating central gaze position. Arrow indicates movement to the right. Time scale at bottom right: 1 sec. Vector plots: Reconstruction of eye movements from vertical and horizontal components. Intersection of axes indicates central gaze position. Dots indicate start, crosses end of saccades. Eye movements (and by inference the approximate target movement) that appear associated with unit burst discharges are shown with heavy lines. Numbers referring to eye positions are cross-referenced to vertical eye movement trace. Note bursts related to saccade sequences and target motion, directed generally upward. Unit records retouched.

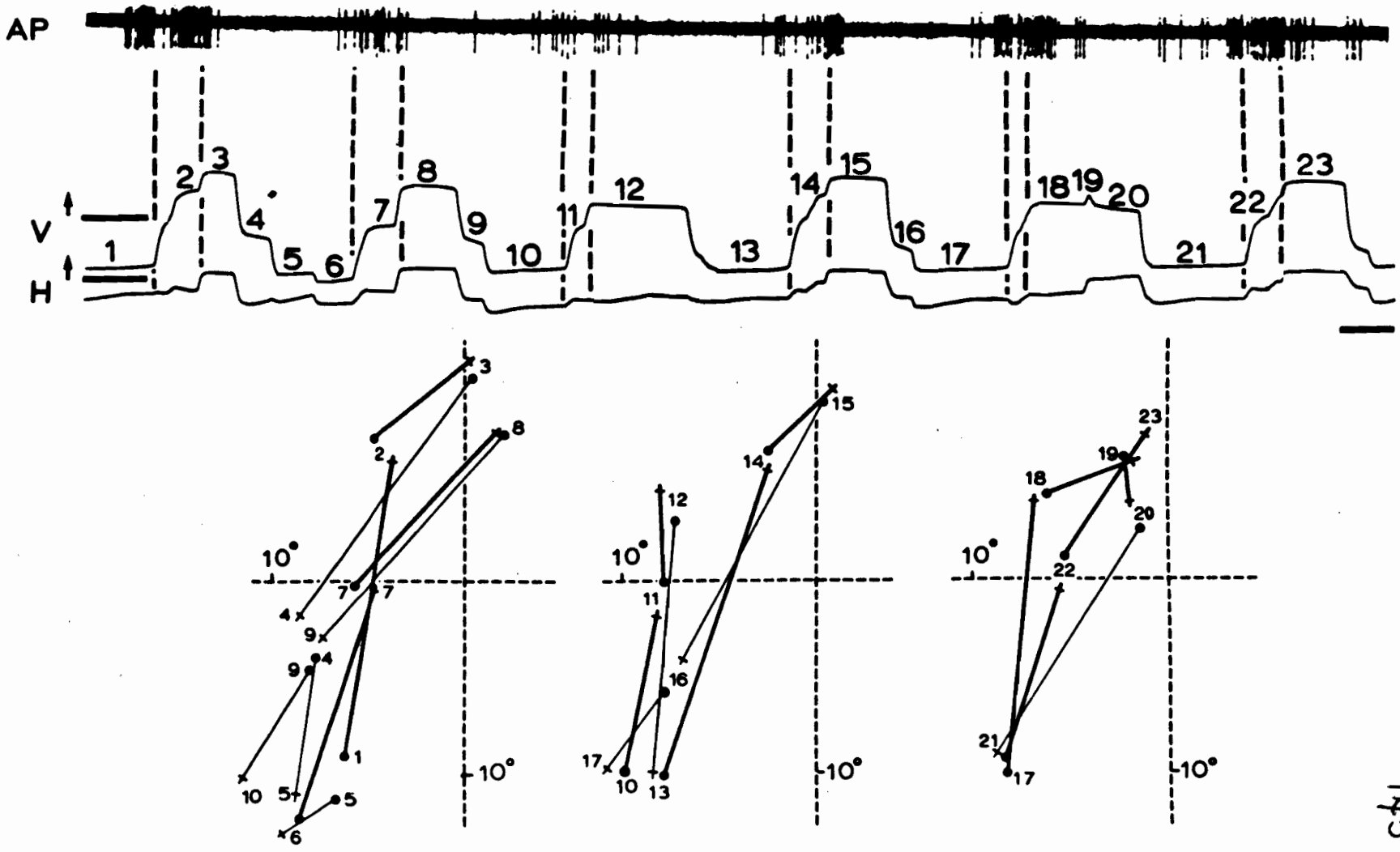
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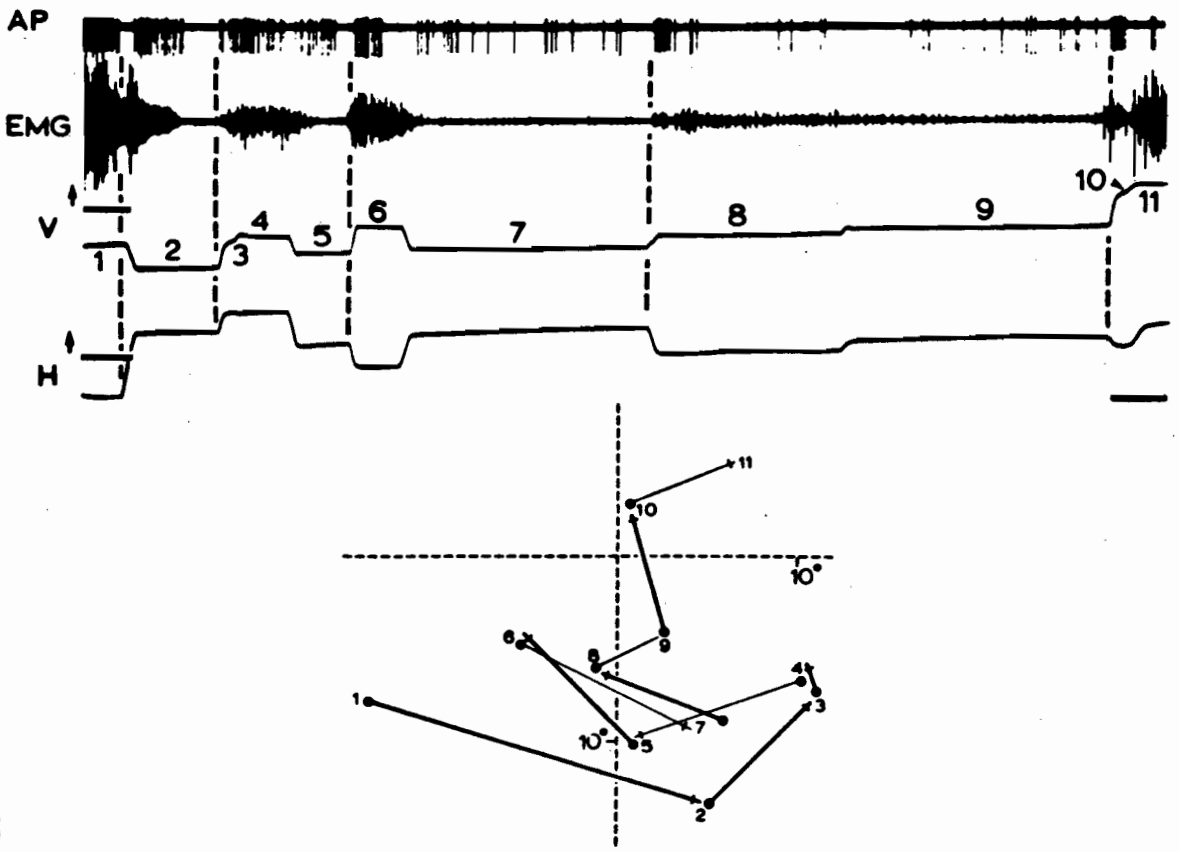
Fig. 2 (Fig. 7-2)

CD cell activity recorded from 'lateral' oculomotor area. EMG: electrical activity in biventer cervicis neck muscle. Other abbreviations as in Fig. 1. A: spontaneous saccades in the dark. B: vestibularly induced nystagmus in the dark. C: nystagmus in the light. D: tracking of target that was moving in a non-specific manner within the visual field. E: tracking of periodically moving target. Note absence of any directional preference in A, B, C, D, but distinct preference for saccades to the right while tracking the periodically moving target in E. Time scale: 1 sec. Unit records retouched.

A



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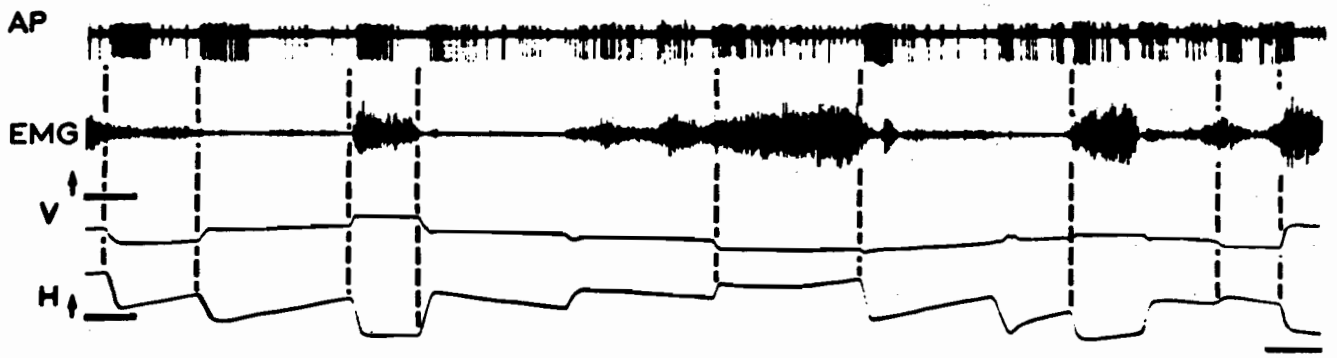

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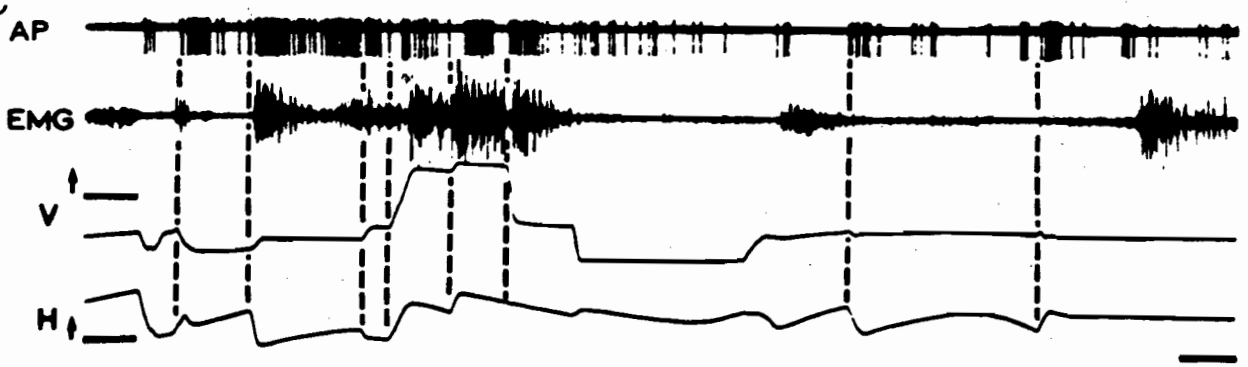

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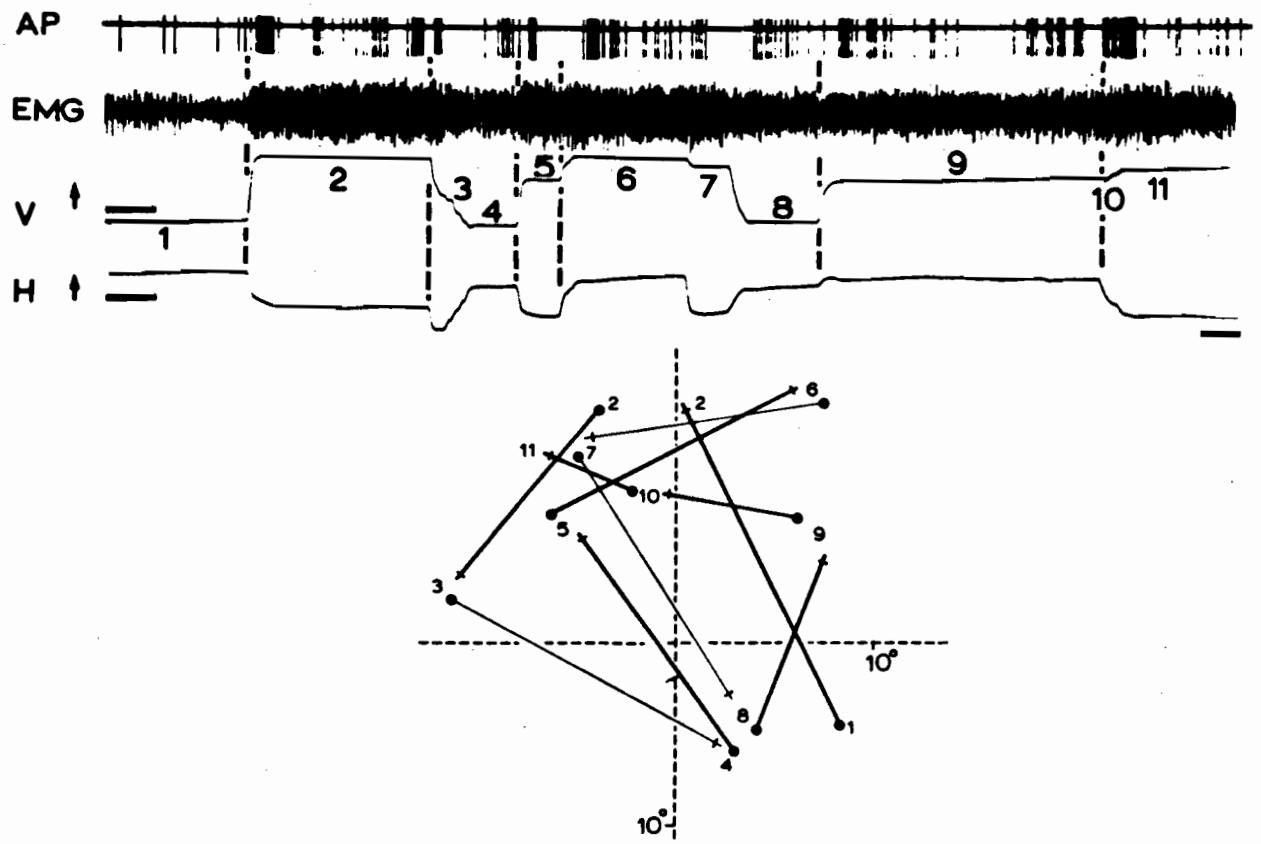
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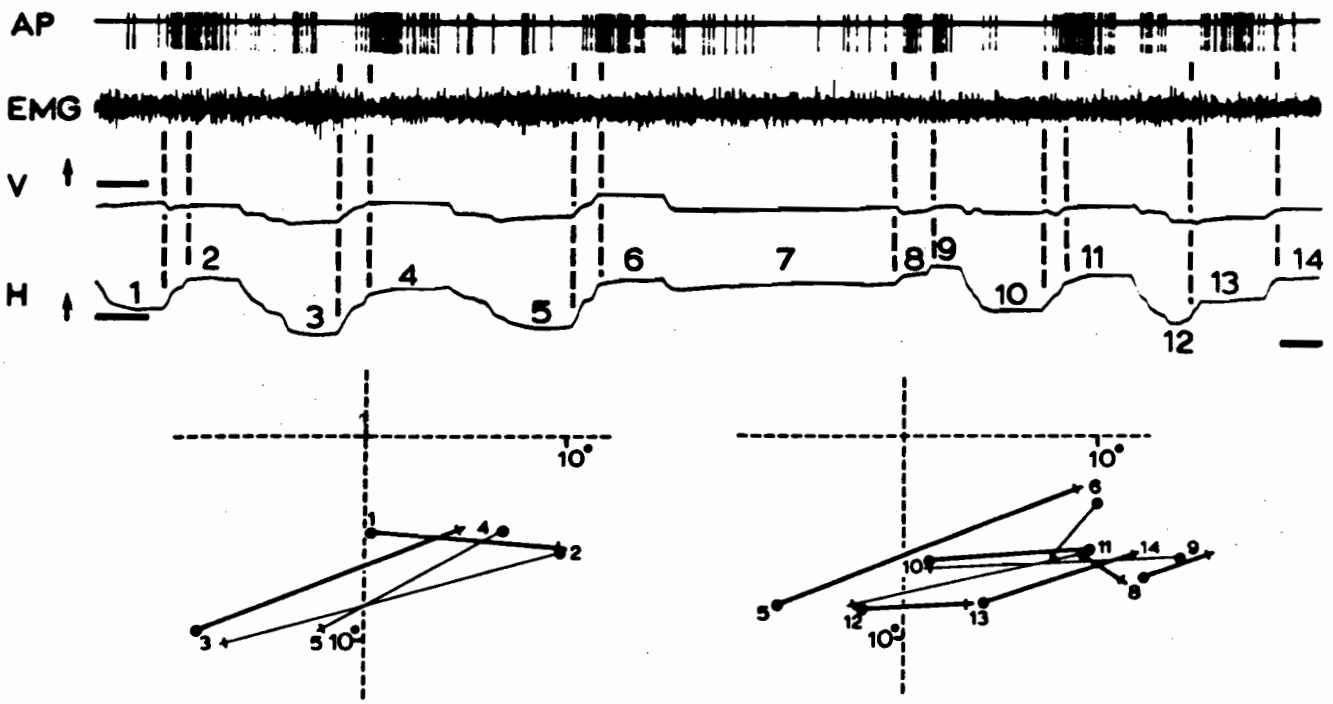
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Fig. 3 (Fig. 7-3)

The transition from a CD cell's non directional discharge pattern to a directional one. Note that during the first left-to-right eye movement cycle, the unit discharged for both directions, whereas during the second and third cycles the discharges became associated predominantly with rightward eye movements. Slight variations in action potential amplitude were due to the animal's straining while trying to track the target. Amplitude scale: 10^{o}. Time scale: 1 sec. Symbols as in Fig. 1.

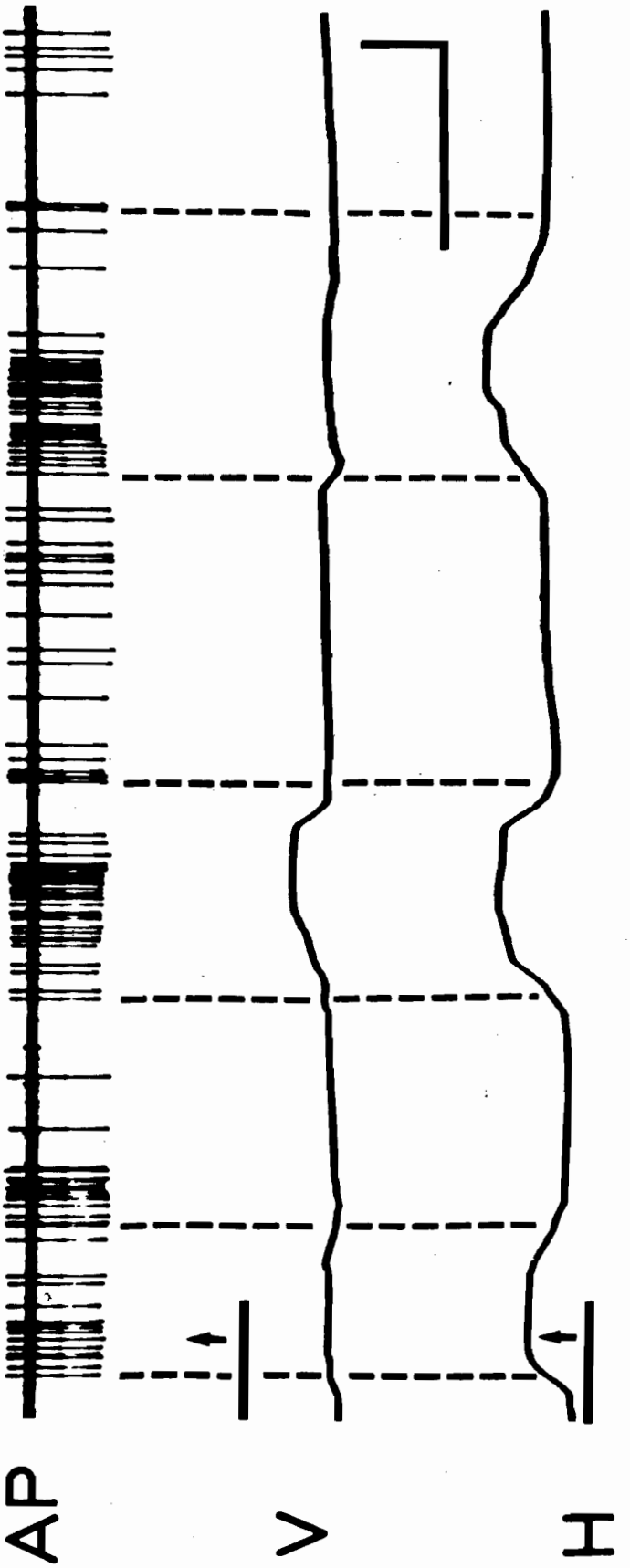
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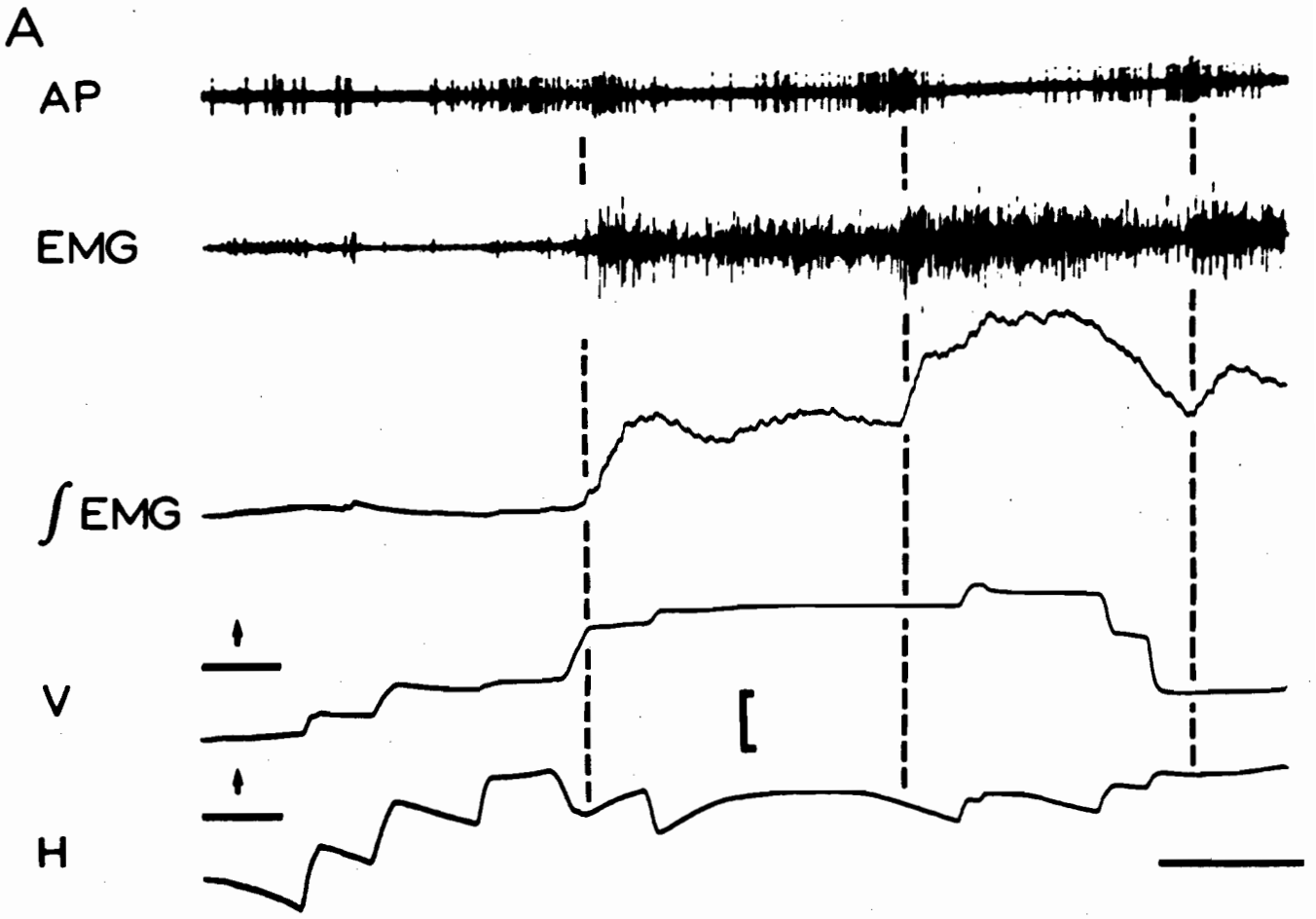
Fig. 4 (Fig. 7-4)

The activity of an N cell, related to the change in the neck EMG. A: $\int$ EMG: rectified and R-C integrated EMG. Other symbols as in Fig. 2. Note that unit discharge is unrelated to eye movements. Amplitude scale: 10 deg. Time scale: 1 sec. B: response of the same cell to stimulation of the contralateral biventer cervicis muscle. Stimulus artefact marked by short bar at beginning of trace. Record retouched. Time scale: 10 msec. C: coronal section through right frontal lobe, some 0.4 mm anterior to the cruciate sulcus. Dot indicates the point in the 'lateral' area from which the activity of this N cell was recorded.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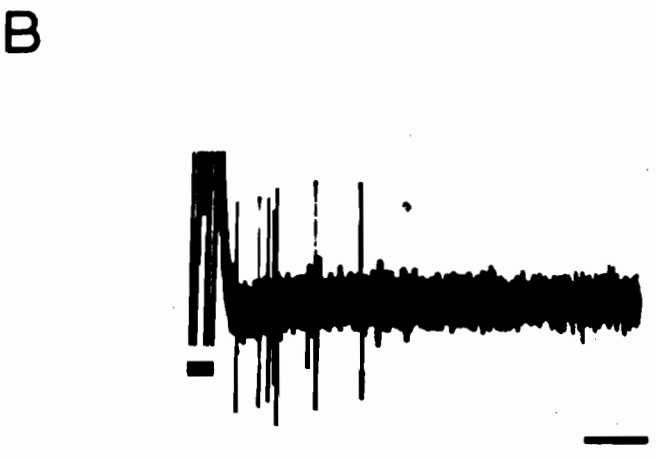
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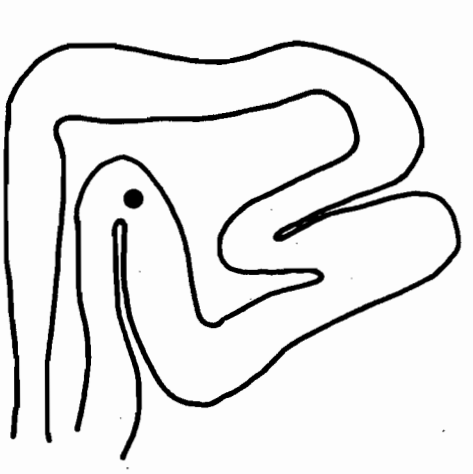
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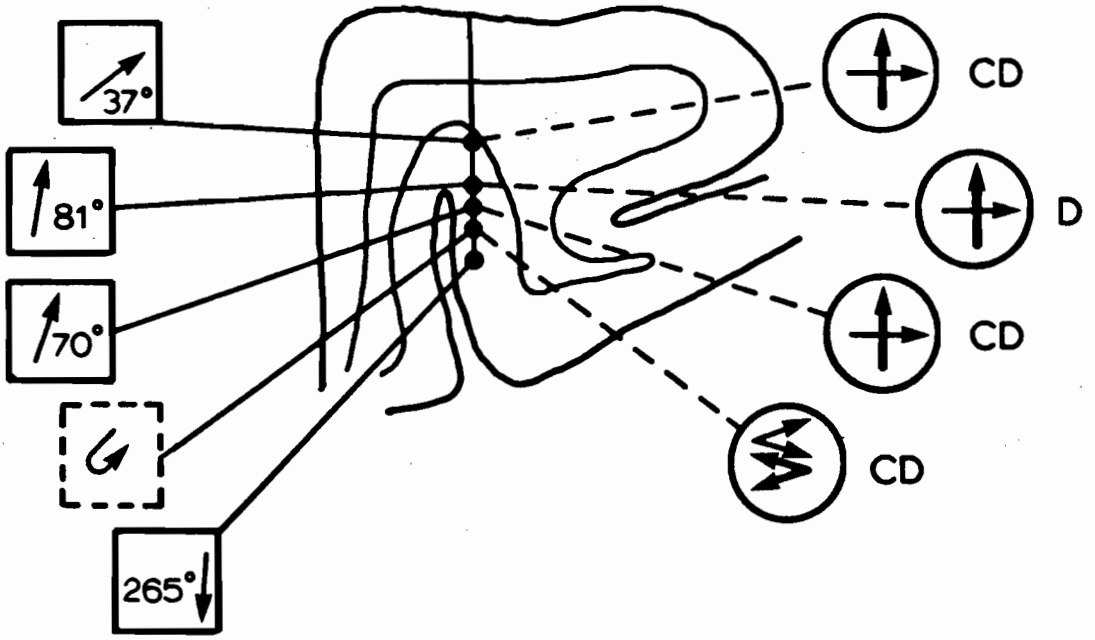
Fig. 5 (Fig. 7-5)

Comparison of the directions of tracking eye movements (circles) preferred by cortical cells, with the direction of eye movements evoked by stimulation (squares) at the points where given cells had just been recorded. A: 'lateral' area: cells at a given cortical point increased their discharge rate when target motion and tracking eye movements were in a direction similar to the one evoked by stimulation of that point. Encircled arrows on the right show the angular range of spontaneous eye movements preferred by the cells. Heavy arrows indicate dominant vector . CD: conditionally directional cell. D: directional cell. The vectors for evoked eye movements are shown, together with average angular directions, in the square boxes on the left. Composite evoked saccades are indicated within the interrupted line square. See text. B: 'medial' area: cells at a given cortical point increased their discharge rate when target motion and tracking eye movements (circles) were in a direction opposite to those evoked by stimulation (squares).

A



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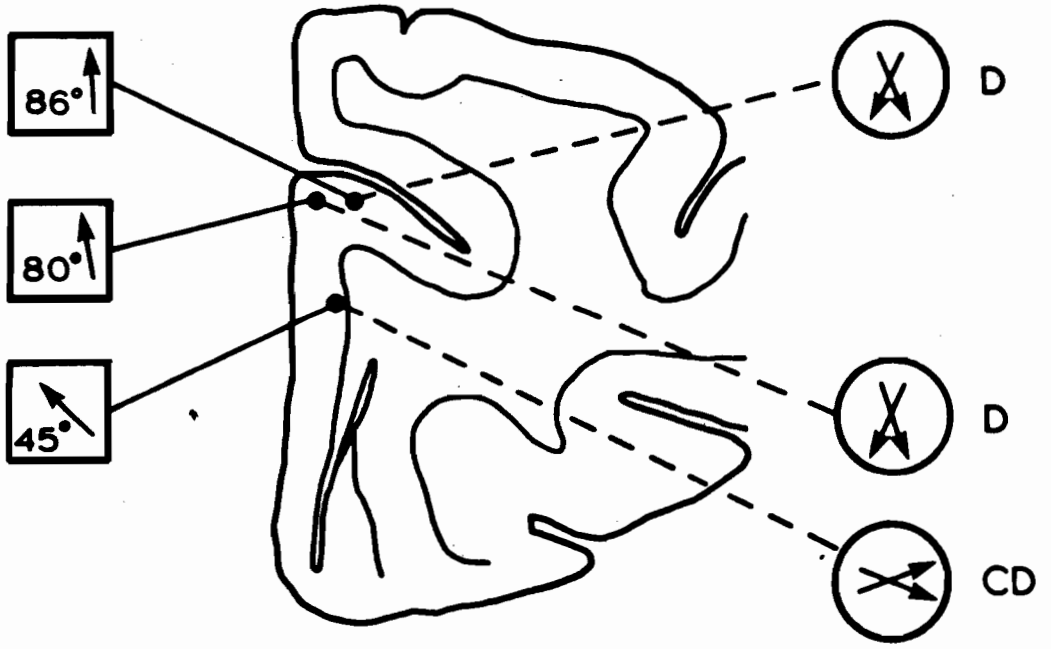

SECTION 4

CORTICO-BRAINSTEM INFLUENCES

CHAPTER 8

SOME EFFECTS OF FRONTAL EYE FIELD STIMULATION ON UNIT ACTIVITY IN THE SUPERIOR COLLICULUS OF THE CAT

Status: This chapter combines the results of the following two short articles by Guitton and Mandl:

Brain Research 68 (1974) 330-334

Expl. Brain Res. Suppl. 1 (1976) 556-561

SUMMARY

(1) The results describe some effects of frontal eye field (FEF) electrical stimulation on unit responses in the superior colliculus of pretrigeminal decerebrate cats.

(2) In both the deep and intermediate layers of the SC, units were found that could be driven by FEF stimulation after a latency ranging between 5-30 msec. These cells were visually unresponsive.

(3) Units were found in the intermediate layers that responded with burst discharges to both FEF and visual stimulation.

(4) In the intermediate layers some visually responsive units were found that had a subthreshold response to FEF stimulation. For these cells the influence of an FEF stimulus could be demonstrated as a distinct modification of their visually evoked responses.

INTRODUCTION

Some forty years ago, Holmes (1938) reported that localized lesions in those parts of the human frontal lobes referred to as "frontal eye field" (FEF) resulted in severe impairments of voluntary eye movements (saccades). It has also been known for some time that stimulation of the FEF in cat and monkey elicits saccadic eye movements (Robinson and Fuchs, 1969; Schlag and Schlag-Rey, 1970; Guitton and Mandl, 1978a, b). One would, therefore, expect cells in that cortical area to discharge prior to voluntary, spontaneously produced rapid eye displacements. This, however, is not the case. It has recently been demonstrated that units whose activity is related to saccades, discharge only after the onset of the eye movement (Bizzi, 1968; Mohler et al., 1973; Guitton and Mandl, 1978b). The latter observation implies that, contrary to previously held opinion, the FEF does not play a role in the initiation of voluntary saccadic eye movements.

The question therefore arises as to the functional significance of the FEF. In the monkey, many neurons within this cortical area have response characteristics which are similar to those found for units in the superior colliculus (SC; Mohler et al., 1973; Wurtz and Mohler, 1976). Furthermore, in both cat and monkey the FEF are known to project to the SC (Sprague, 1963; Künzle et al., 1976). One may ask, therefore, whether saccade related discharges of FEF cells might interact with visual responses of cells in the SC; either during single saccades or during tracking (Guitton and Mandl, 1978b).

The experiments described here were undertaken to investigate the possible convergence and interaction of retinal and FEF inputs upon single cells in the SC. It was the particular aim of this work to demonstrate that

FEF stimulation can modify the activity of SC cells responding to moving visual stimuli.

METHODS

Mid-pontine pretrigeminal cat preparations were used. In the cat, the FEF in each hemisphere consists of two regions, one along the mesial face just below the cruciate sulcus, and the other in the depth of the presylvian sulcus. Both regions within a given hemisphere yield eye movements in response to electrical stimulation. The tip of the stimulating electrode was aimed at those specific areas within the grey matter of the FEF where previous work (Guitton and Mandl, 1978a,b) with awake, chronic cats had shown that: (a) well defined, reproducible saccadic eye displacements could be elicited; and (b) single unit discharges, related to specific directions of spontaneous eye movements, could be recorded. Subsequent histological controls confirmed that all stimulated points were located within one of the two (medial or lateral) FEF regions described by Schlag and Schlag-Rey (1970) and Guitton and Mandl (1978a). To facilitate accurate electrode placement, these regions were explored for sites yielding eye movements in response to electrical stimulation. Trains of pulses lasting 200 msec, with a frequency of 100 pulses/sec, and pulse durations of 500 μsec, were used. The stimulating current never exceeded 300 μA, and was so adjusted that eye movements were just visible. The stimulating electrode was then left in place. The animal was then paralysed with gallamine triethiodide (Flaxedil) and provided with forced ventilation. Dark-light moving patterns (dots, lines, borders) were projected onto a tangent screen some 30 cm in front of the cat and the images brought to a focus on the animal's left retina by means of extraocular lenses. The

right eye was occluded. A tungsten recording microelectrode was introduced into the right SC, at an angle of 30° to the sagittal plane. During the search for units the right FEF was continuously stimulated with single pulses. Once a unit was found FEF stimuli consisting of either a single pulse or a train of 2-14 impulses at a frequency of 200 Hz, were applied once every 2-4 seconds either independently, or at various times before and after the onset of a moving visual stimulus. Stimulating currents ranged between 50-400 microamperes. The magnitude of a collicular cell's response to a given combination of stimuli was quantitatively determined by adding the discharges (above control level) generated by the cell during a fixed number of response cycles (Fig. 5). It was found that this made for a more reliable and consistent quantitative measure of response magnitude, as compared to measures based on peristimulus histogram peaks.

The FEF of monkey is known to project to the SC (Künzle et al., 1976). A similar projection has been reported for cat (Sprague, 1963) but the results of that experiment are unclear due to the concise nature of the report. Consequently, a verification of the pathway from SC to FEF was undertaken by stimulating the deep layers of the SC and recording antidromic responses in the FEF.

A number of units in both the medial and lateral FEF were identified as relaying directly to the ipsilateral SC. An antidromic response was verified by assuring that: (1) the latency, following a shock to the SC, was constant; and (2) the unit could follow faithfully stimulus trains of frequency 100 Hz. The latencies of such identified antidromic FEF responses were within the range of 4-7 milliseconds. As such antidromically driven units were located in FEF regions where stimulation is known to

elicit eye movements and/or collicular responses, they were taken as further evidence for the existence of a direct functional link between FEF and SC.

RESULTS

A total of 27 collicular units that were studied responded in some way to FEF stimulation.

Units that responded to only FEF stimulation

In both the deep and intermediate layers of the SC, 15 single units were found that could be driven by FEF stimulation, with response latencies within the range of 5-30 milliseconds. These units were visually unresponsive, and generated action potentials that were considerably smaller than those originating from visually responsive cells. An example of this type of response is shown in Fig. 1. Fig. 1A shows a coronal section through the right frontal lobe, 2 mm behind the cruciate sulcus as measured on the dorsal surface of the brain. Dark points indicate the sites from which eye movements could be elicited. The investigated unit was located 2 mm below the collicular surface (Fig. 1B) and responded to stimulation of the point marked S in Fig. 1A. This response consisted of a burst of activity, which on the average peaked 10 msec after the electrical pulse was applied to the FEF (Fig. 1C).

In some cases, visually responsive SC cells were found immediately adjacent to the small FEF driven cells (i.e. both types recorded with one electrode). This is shown in Fig. 2. In part A stimulation of the FEF with a single pulse evokes a burst of activity with a latency of some 10 msec. In Fig. 2B a visual stimulus is swept across the receptive field of a visually responsive cell recorded simultaneously with the unit whose discharge is shown in Fig. 2A. It is observed that the small unit has no

response to visual stimulation. As a control, Fig. 2C, both the FEF and visual stimuli are applied nearly simultaneously and it can be seen that again each unit responds to its "preferred" stimulus. Fig. 3 shows another type of collicular unit that responded to FEF stimulation but was visually unresponsive. This cell was recorded 2.1 mm below the collicular surface and was influenced by stimulating the point marked S, shown in the coronal section taken 4.5 mm behind the right cruciate sulcus (Fig. 3A). This cell was silenced for a 100 msec period, beginning approximately 10 msec after the electrical stimulus to the FEF. The unit then showed a burst of activity again followed by a silent period, and then a return to its previous level of spontaneous activity.

Units that responded to both FEF and visual stimulation

Only two units were found that responded with spikes to both FEF and visual stimulation; both of these units were found in the intermediate layers of the SC. One example, shown in Fig. 4, was found 2.7 mm below the collicular surface. In the upper trace it can be seen that there is a short latency response (5-8 msec) to a single shock applied to the FEF. (Five superimposed traces are shown). This unit also responded to visual stimulation. The response as judged by the display of neural activity on a storage monitor oscilloscope, was best to slow ($\simeq 10^{o}$/sec) movements. At this velocity a vigorous burst of activity was observed whereas at higher stimulus speeds only a few action potentials could be evoked.

Units that had a subthreshold response to FEF stimulation

The influence of FEF stimulation upon visually responsive SC cells could be demonstrated most often as a distinct modification of their visually evoked responses. For these units an FEF stimulus alone had a subthreshold effect and did not elicit action potentials. Such cells were found more superficially than those responding to FEF stimulation alone, i.e. about 1.3-2.2 mm below the collicular surface. Figure 5 represents a specific example of the type of interaction observed.

When a single electrical shock applied to an identified region of the medial FEF preceded the visual response of this SC cell by 10-100 msec, a change in the cell's visual control response could be observed. The visual response, elicited by a dark "tongue" moving at 200 deg/sec across the receptive field, was enhanced when the FEF stimulus preceded the visual response by some 10-20, or 80-100 msec. In the midrange of 30-70 msec, the response was depressed (see Fig. 5). This effect was observed with cells in the intermediate SC layers. It should also be noted that the effect of FEF stimulation upon the visual response appeared when the FEF stimulus preceded the visual response by as little as 10 msec, implying a minimum latency of no more than 10 msec for the initial FEF-SC interaction. The timing, magnitude, and sign of the interaction illustrated in Fig. 5, varied from cell to cell.

The results in Fig. 5 show that the normal visual response of an SC cell can be either elevated or suppressed depending on the timing of the FEF pulse. This effect also can be demonstrated by applying a train of varying duration to the FEF and monitoring the response of the affected collicular unit. This is shown in Fig. 6 for a cell different than the

one shown in Fig. 5. The unit's response to a visual stimulus alone is shown in trace A. Trace E shows the control visual response taken at the end of the complete test. In B it can be seen that the visual response is increased when the FEF stimulus consists of a single pulse preceding the visual response by some 100 msec. However when the FEF stimulus is changed to a train of pulses (200 Hz, 500 microsecond pulse width) lasting some 60 msec, the visual response is completely suppressed in the first 200 msec following the initiation of the FEF volley.

DISCUSSION

How do these results, obtained in acute preparations, relate to FEF-SC interaction in the intact animal? The present evidence, together with data originating from experiments with chronic animals (Guitton and Mandl, 1978a,b), supports the view that saccade related neural activity in the FEF may influence the discharges of visual cells in the tectum; and that this influence may be mediated via the histologically demonstrated direct link between prefrontal cortex and superior colliculus.

Nevertheless, some of the observed results may have been mediated by pathways other than the direct one. Within this context, the potential neural link extending from the FEF via the parietal lobe (area 7) to the deeper layers of the SC (Petras, 1971; Künzle and Akert, 1977) deserves consideration. In addition to that Spatz (1976), and Spatz and Tigges (1972; 1973) have shown that the middle temporal visual area in primates (MT, possibly homologous with Clare-Bishop area in the cat) has afferents from FEF and projects to SC. Furthermore, the possibility that some of the long latency effects of FEF stimulation have been mediated by routes involving the striatum, thalamus and reticular formation cannot be discounted (Orem and

Schlag, 1971; Schlag and Schlag-Rey, 1971; Fuller, 1975). These considerations are particularly relevant, in view of the observation that some of the effects produced in cells of the SC by FEF stimulation may occur after latencies of up to 200 msec.

A further point to be considered is the intensity of stimulating currents employed in this study. It is undoubtedly true that currents of such magnitude (50-400 microamperes) pose difficulties when assessing the likely extent of the neural substrate affected by the stimulus. Nevertheless, it appears that each FEF stimulus exerted its characteristic modulating effect within the context of a specific electrode position within the FEF. The following observations, made with awake, chronic animals (Guitton and Mandl, 1978a), bears upon this point: (1) Single unit discharges recorded within a given FEF area were associated with spontaneous saccades whose direction bore a consistent relation to the direction of evoked saccades produced by electrical stimulation of that same FEF area. This observation implies a functional link between the activity of units in a given FEF region, and the type of eye movements that can be elicited by electrical stimulation of that same region. (2) The type of eye movements evoked by stimulation at one given point within the FEF could be reproduced in several animals. (3) Furthermore, displacing the stimulating electrode tip by less than 0.5 mm could significantly, and reproducibly, change the characteristics of evoked eye movements.

The present results, applied to the intact animal, hint at the possibility that neural discharges originating in the FEF during voluntary eye movements may substantially modify the activity of visual cells in the SC. Future work should aim at verifying this hypothesis in alert behaving animals and at determining its functional significance.

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Fig. 1 (Fig. 8-1)

Unit in superior colliculus (SC) responding only to frontal eye field (FEF) stimulation. A: coronal section of the right frontal lobe cut 2 mm caudal to the cruciate sulcus as it appears on the dorsal surface of the brain. Vertical straight line through the section represents the stimulating electrode track. Black circles (●) indicate sites where stimulation elicited eye movements. S indicates site where electrical stimulation elicited responses in the SC; scale bar, 1 mm; COR, coronal sulcus; CR, cruciate sulcus; PR, presylvian sulcus. B: coronal section through the SC at stereotaxic coordinate A 2.0. Microelectrode track is shown penetrating the SC at an angle of 30^{o} to the sagittal plane. R indicates the site of recording. SC, superior colliculus; scale bar, 1 mm. C: average response histogram of the unit's response to 54 consecutive FEF stimuli, timed 2 sec apart.

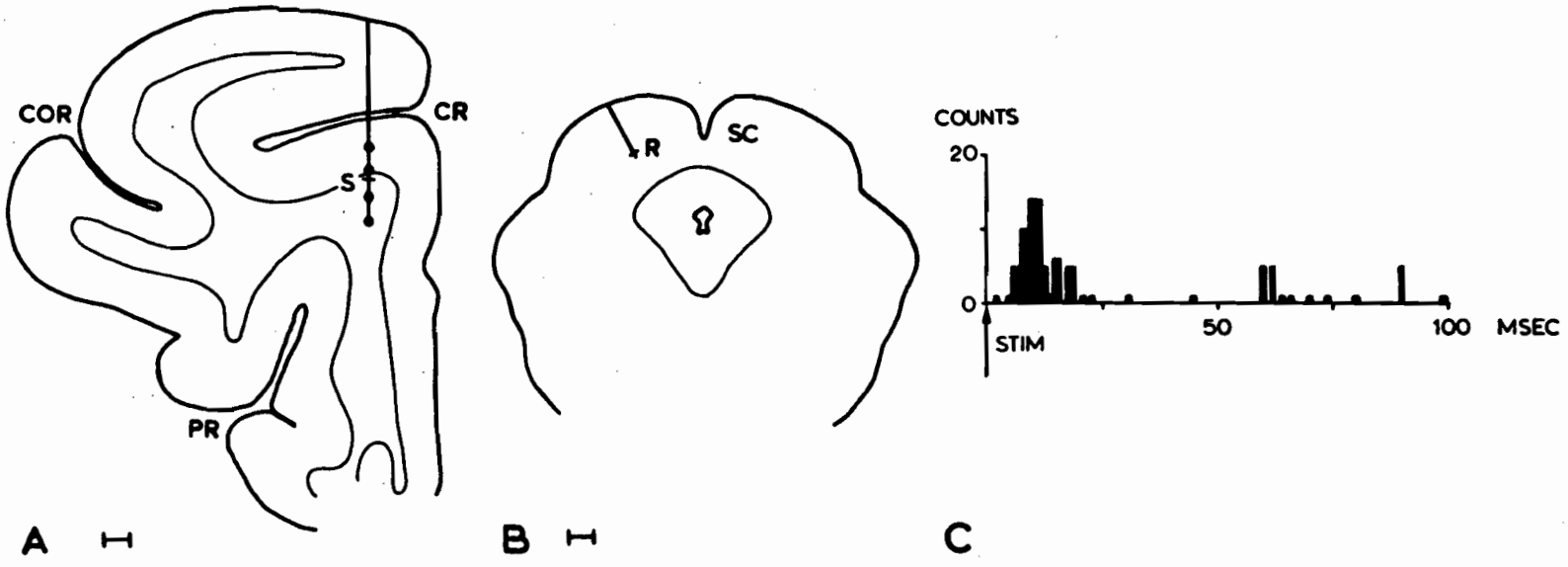

COR
CR
S
PR
R
SC
COUNTS
20
0
STIM
50
100
MSEC
A
B
C

Fig.2 (Fig. 8-2)

Two units recorded simultaneously in the superior colliculus. In A the small unit discharges with a burst following stimulation of the FEF with a single pulse. In B a larger unit responds to a visual stimulus consisting of a dark tongue sweeping across the receptive field. The time during which the visual stimulus is in the receptive field is indicated by the black bar under the trace. In C both the FEF and visual stimuli are applied nearly simultaneously. Both units are seen to discharge, each to its own "preferred" stimulus.

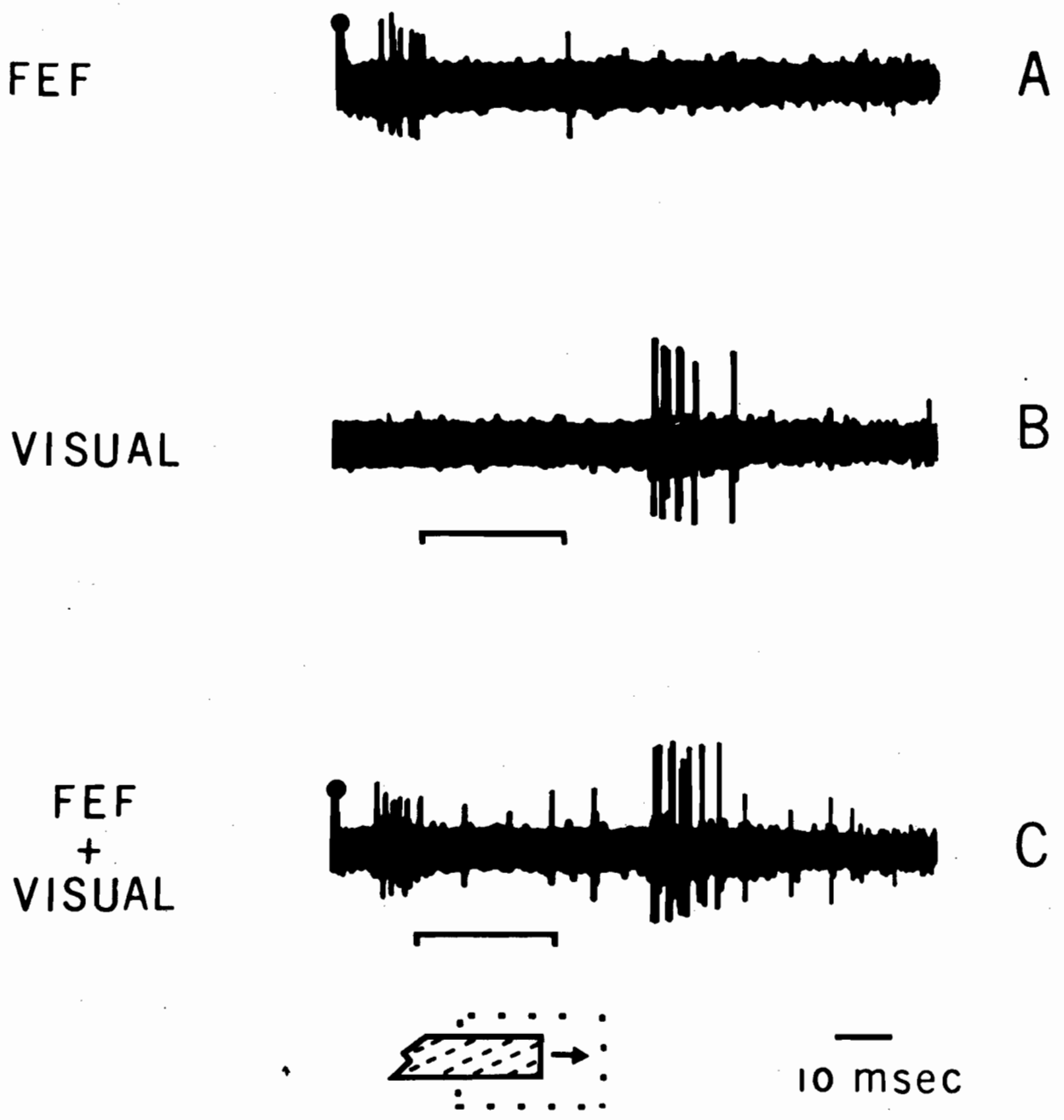

FEF
A
VISUAL
B
FEF
+
VISUAL
C
10 msec

Fig. 3 (Fig. 8-3)

Unit in superior colliculus (SC) responding only to frontal eye field (FEF) stimulation. A: coronal section of the right frontal lobe cut 4.5 mm caudal to the cruciate sulcus as it appears on the dorsal surface of the brain. Vertical straight line through the section represents the stimulating electrode track. Black circles (●) indicate sites where stimulation elicited eye movements. S indicates site where electrical stimulation elicited responses in the SC; scale bar, 1 mm; COR; coronal sulcus; CR, cruciate sulcus; MAR, marginal sulcus; PR, presylvian sulcus; ECT, ectosylvian sulcus; B: coronal section through the SC at stereotaxic coordinate A 2.0. Microelectrode track is shown penetrating the SC at an angle of 30^{o} to the sagittal plane. R indicates the site of recording. SC, superior colliculus; scale bar, 1 mm. C: average response histogram of the unit's response to 90 consecutive FEF stimuli, timed 2 sec apart.

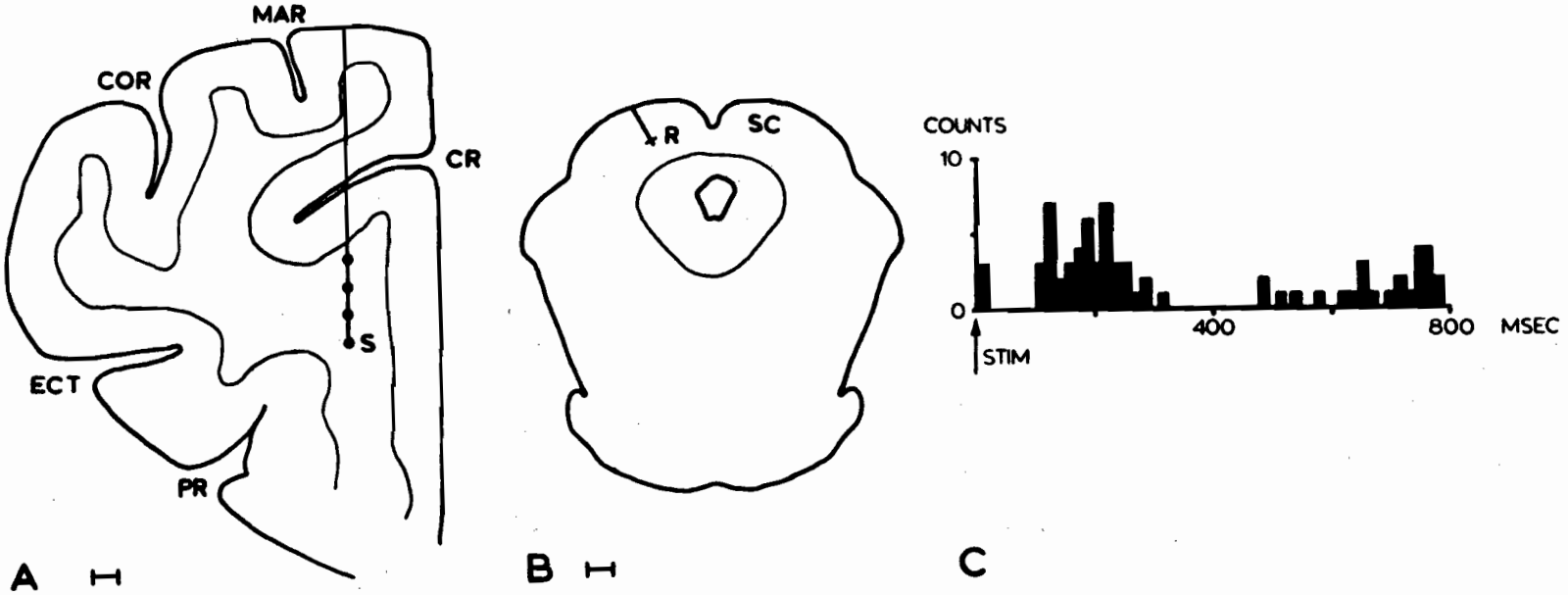

MAR
COR
CR
S
ECT
PR
A
R
SC
B
COUNTS
10
0
400
800
MSEC
STIM
C

Fig. 4 (Fig. 8-4)

Unit in the superior colliculus that responded to both FEF and visual stimulation. The top trace shows the response to a single shock applied to the ipsilateral FEF (five superimposed responses). The bottom trace shows the unit's visual response to a black border moving slowly across the cell's receptive field. Optimal response was to slow movement of the stimulus.

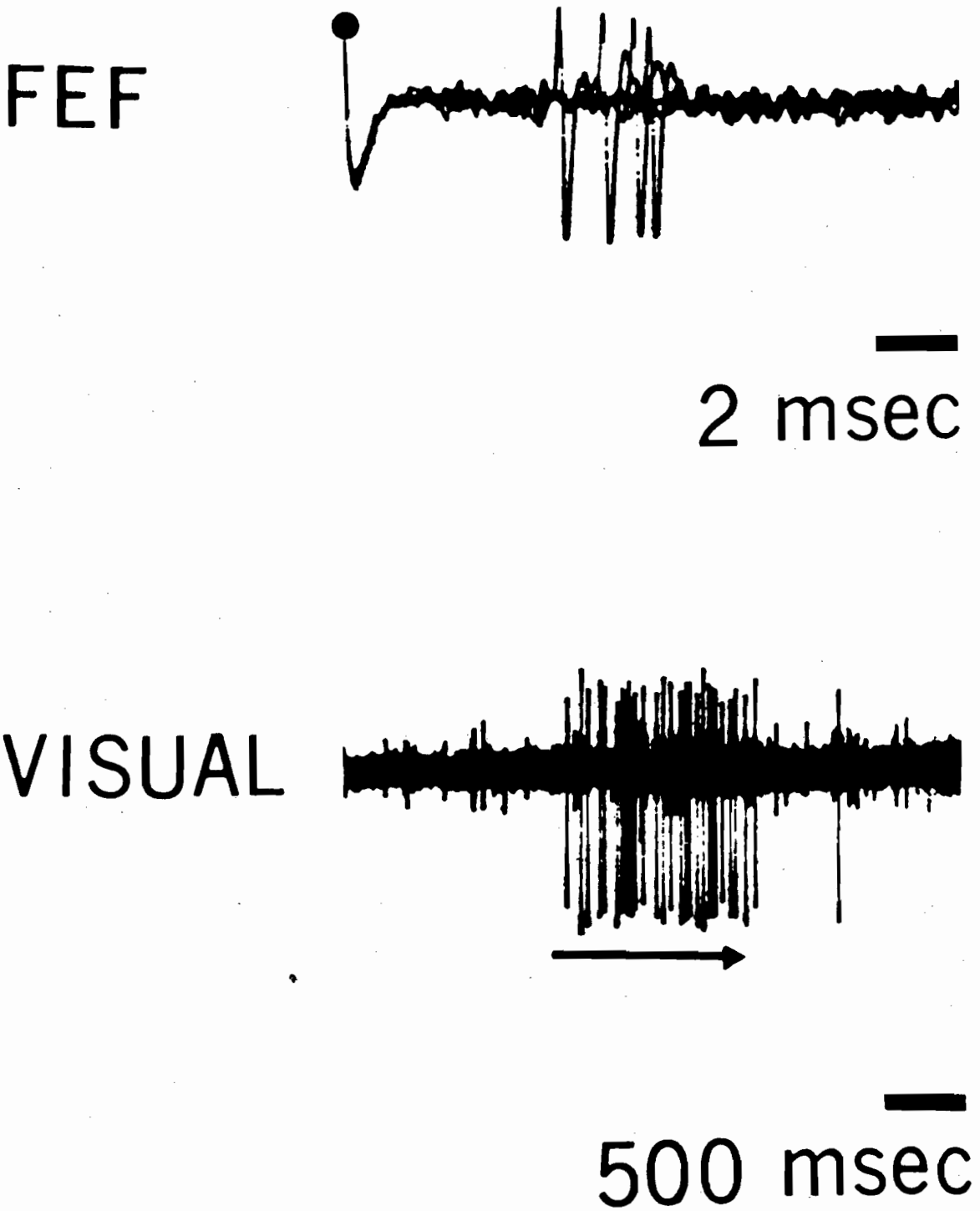

FEF
2 msec
VISUAL
500 msec

Fig. 5 (Fig. 8-5)

The interaction of visual and FEF stimuli on a single cell in the intermediate layers of the superior colliculus. The visual stimulus consisted of a dark "tongue" moving at approximately 200 degrees/sec through the cell's receptive field. The electrical stimulus to the right FEF consisted of two current pulses (300 microamperes) separated by a 5 msec interval.

Abscissa: The time interval, in milliseconds, by which the electrical FEF stimulus preceded the cell's visual response (the cell's latency in response to only the visual stimulus was approximately 50 msec).

Ordinate: The normalised response of the cell to the combined visual and FEF stimulation. Each point on the graph represents the sum of twenty cell responses. Note that the cell's response is maximally depressed when the stimulus to the FEF precedes the visual response by some 40-50 msec. Assuming a 50 msec latency for the visual response, this would indicate that the cell's visual response is smallest when FEF unit activation coincides with the visual stimulus. The ordinate is interrupted by three open circles. These represent control tests made of the unit's response to only a visual stimulus and taken before, in the middle, and at the end of the experimental run.

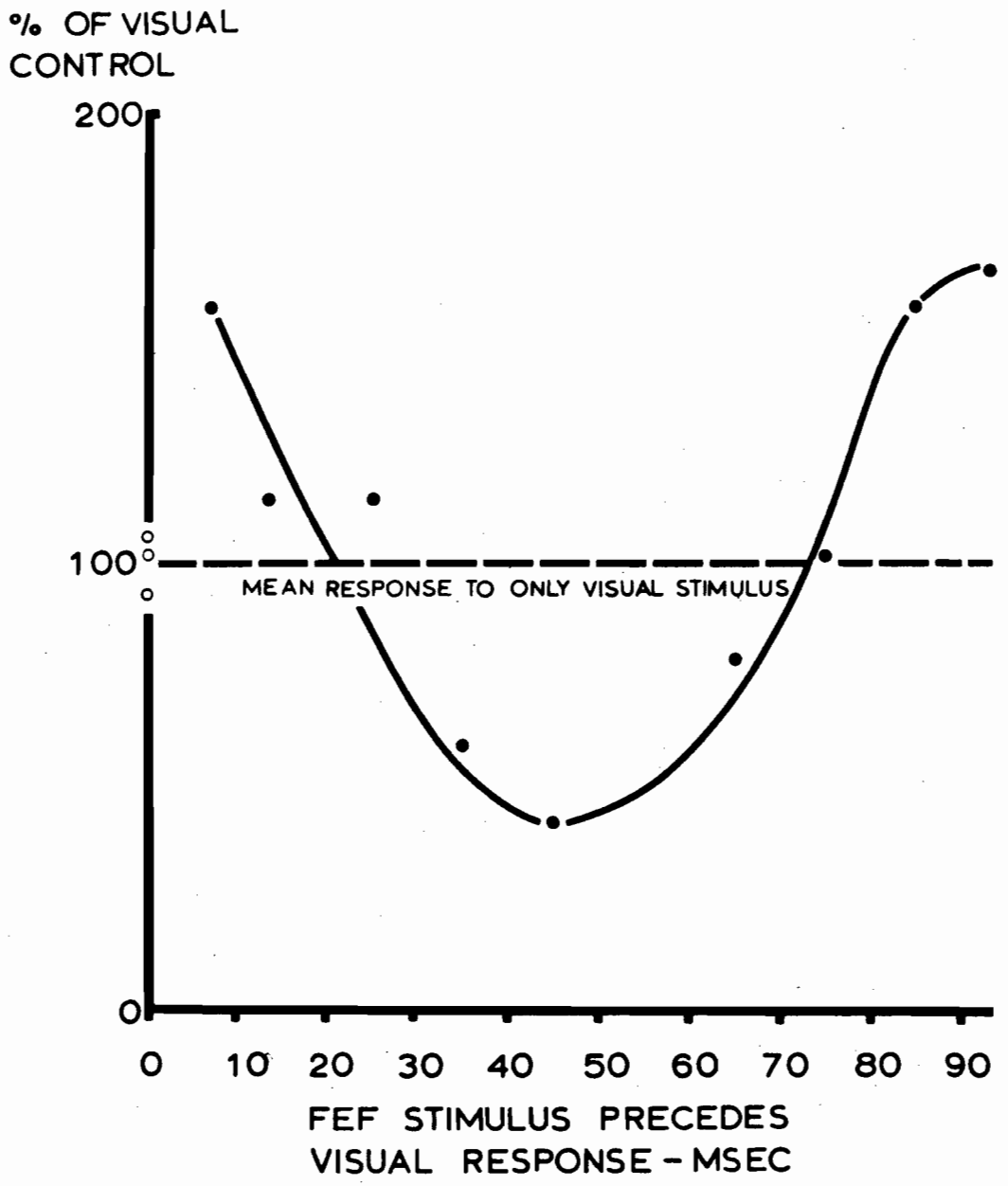

% OF VISUAL CONTROL
200
100
0
MEAN RESPONSE TO ONLY VISUAL STIMULUS
0
10
20
30
40
50
60
70
80
90
FEF STIMULUS PRECEDES VISUAL RESPONSE - MSEC

Fig. 6 (Fig. 8-6)

Modification of the visual response of a collicular cell recorded in the intermediate layers, depending on whether the FEF stimulus is a pulse or a train of pulses. In A, C and E are shown the control visual responses taken respectively at the beginning, middle and end of the test. In B the visual response is enhanced when a FEF single pulse precedes the visual response by some 100 msec. In D the visual response is blocked when the FEF stimulus is changed to a train 60 msec in duration.

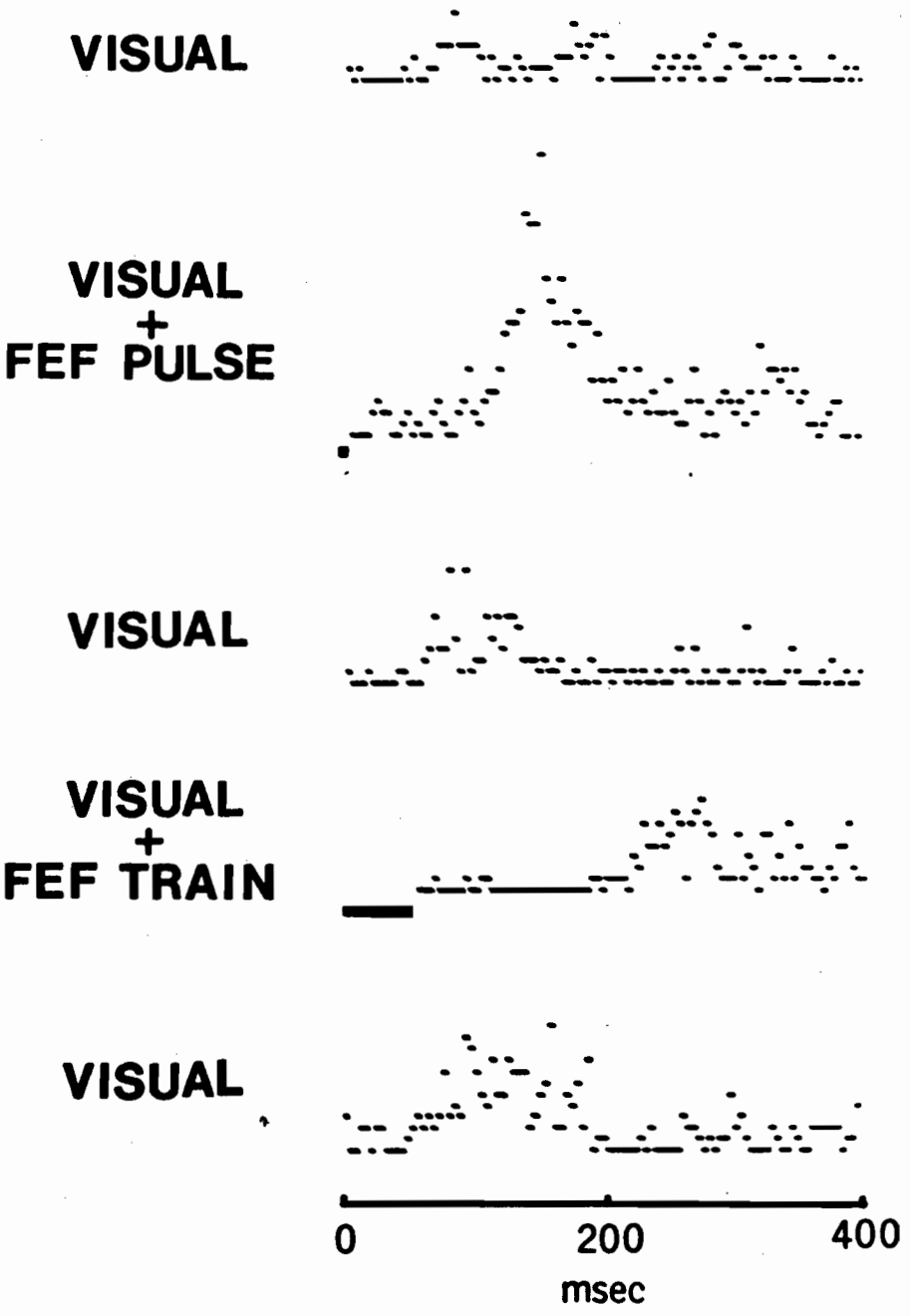
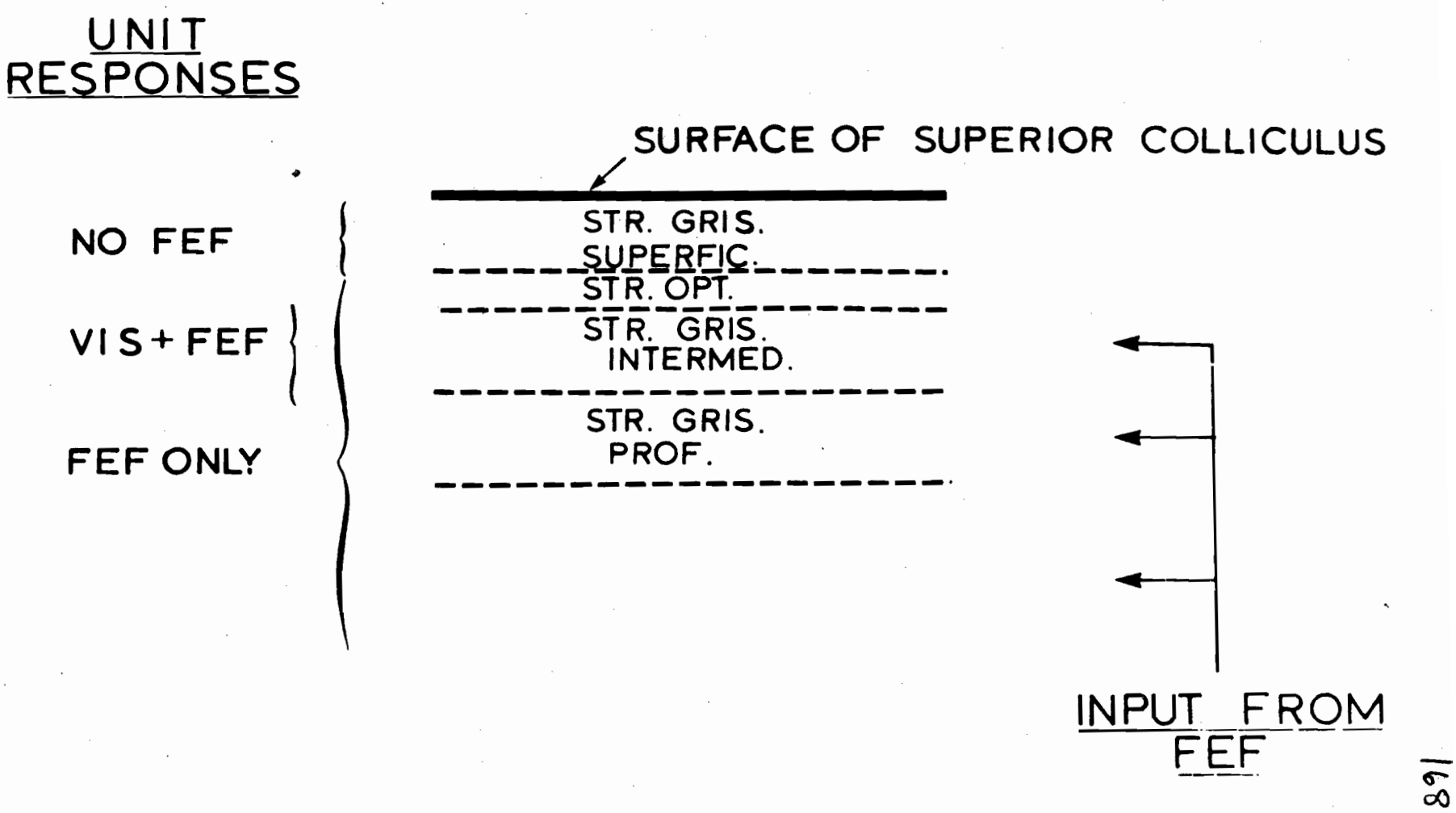

VISUAL
A
VISUAL
+
FEF PULSE
B
VISUAL
C
VISUAL
+
FEF TRAIN
D
VISUAL
E
0
200
400
msec

Fig. 7 (Fig. 8-7)

Vertical distribution of collicular units classed according to whether: (1) they do not respond to FEF stimulation (NO FEF); (2) their visual response is modified by FEF stimulation (VIS + FEF); or (3) they respond to only FEF stimulation (FEF ONLY). On the right, the arrows indicate the site of termination of FEF afferents (Sprague, 1963).


UNIT RESPONSES
SURFACE OF SUPERIOR COLLICULUS
NO FEF
VIS + FEF
FEF ONLY
STR. GRIS. SUPERFIC.
STR. OPT.
STR. GRIS. INTERMED.
STR. GRIS. PROF.
INPUT FROM FEF
891

SECTION 5

SUMMARY, CONCLUSIONS, AND CONTRIBUTIONS TO KNOWLEDGE

CHAPTER 9

SUMMARY AND CONCLUSIONS

SUMMARY AND CONCLUSIONS

The general aim of the work presented in this thesis has been to provide greater insight into cortical and cortico-brainstem processes that, for the cat, are implicated directly in oculomotor control. The frontal eye field (FEF) is a cortical region that has long been considered important in the mediation of voluntary eye movements; and it has been tempting to speculate that this frontal lobe area exerts an important influence on brainstem controlled reflexive eye movements. The experiments presented herein have dealt essentially with the FEF and its descending projection into the superior colliculus (SC), and have considered the role of these entities in the control of saccadic eye movements.

Before embarking on the FEF project, a number of studies were undertaken with the particular aims of furnishing information on the rapid eye movements of the cat. This work was judged essential because at the time the FEF exploratory recording sessions were begun (1974) virtually nothing was known about the normal repertoire of ocular movements in this species.

The studies on eye movements presented in this thesis were greatly aided by the use of an accurate method for recording eye movements. This technique was first developed by Robinson (1963) and makes use of the principle that a coil of wire wound about the eye, and subjected to a magnetic field, will produce a signal related to the angle the eye makes with respect to this field. The method is called "the eye coil in magnetic field technique". At the onset of the experimental program, a novel electronic system, based on frequency coding, was developed as an alternative to the more expensive systems available at that time; all of which were based on phase coding. The basic principles of the new system are described in Chapter 2.

The studies of rapid eye movements in cat were described in Chapters 3 and 4. The experiments began with a comparison between saccades and quick phases of vestibular nystagmus. These two types of rapid movement were found to be the same suggesting that the slow phase signal of vestibularly induced nystagmus actually pauses during the quick phase (Chapter 3). Following this, an analysis was made of how horizontal and vertical saccades are combined to produce an oblique movement. It was found that the smaller of the two orthogonal (horizontal and vertical) components of oblique saccades made in the light, tends to have a duration equal to that of the larger component. This is different than the duration this short component would have if it existed alone as a pure movement. These results have suggested an important link between the horizontal and vertical channels of the oculomotor system. Furthermore, this link appears somewhat weakened when oblique saccades are made in the dark (Chapter 4).

Armed with this knowledge about the cat's normal repertoire of rapid eye movement, plus a well tested new system for precisely recording ocular movements,the experiments on the FEF were begun.

The FEF of cat was taken to be a region of the frontal lobe where eye movements could be elicited by electrical stimulation. In cat, eye movements may be evoked from a number of frontal zones but among these, the medial wall of the hemisphere and the medial and lateral banks of the presylvian sulcus are normally referred to together as the cat FEF. The results were obtained by stimulating and recording from the FEF of alert cats whose heads were fixed. The following basic questions were asked. Do cells in the FEF of cat discharge in association with voluntary eye movements (i.e. saccades)? Do some cells have characteristic discharge

properties related specifically to the behavioural act of tracking? (Note that perseverative tracking appears to be one long term deficit associated with FEF lesions). How do eye movements associated with burst discharges of a specific unit compare to saccades evoked by electrical stimulation applied at the site where the unit has just been recorded? The experimental results are described and discussed in Chapters 6 and 7. A summary is given below and a comparison is made, when possible, with information available for monkey (see Figs. 1 and 2, and Table 1).

Stimulation of the FEF

On the basis of latency and type of evoked eye movement it was possible to sub-divide the cat FEF into two regions: the "lateral" area which encompasses the lateral wall of the presylvian sulcus; and the "medial" area which includes both the medial wall of the hemisphere below the cruciate sulcus, and the medial bank of the presylvian sulcus.

Stimulation of "medial" area in normal alert animals yielded all or nothing oblique saccades directed contralaterally. This is similar to what is observed during stimulation of monkey FEF (Robinson and Fuchs, 1969). The latency of the evoked movements was on the average 45 msec; the shortest latency being about 25 msec. In monkey, the average and shortest latencies were 25 msec and 15 msec respectively (item 4 of Table 1). The amplitude and direction of saccades evoked in the "medial" area were independent of initial eye position and only depended on the cortical site being stimulated. Amplitude changes were small between stimulated cortical points and it was a variation in the direction of evoked saccades that was most evident. By contrast, in monkey FEF, mainly horizontal eye movements are evoked and

it is amplitude that varies with cortical site (see also Table 1).

In the cat "lateral" area the evoked saccades tended to be ipsilateral in the more anterior region whereas more posterior, they were directed towards the central gaze position. Centering or ipsilateral movements have not been evoked from monkey FEF. In the "lateral" area, the threshold for evoking eye movements (50 μA) was greater than that for evoking neck muscle EMG activity. In the "medial" area the thresholds for both were similar (50 μA). In both areas, when saccades and neck EMG activity were evoked together, the EMG preceded the eye movement.

Evidence supporting the subdivision of cat FEF into the "medial" and "lateral" areas has been presented by a number of other workers. Mention has already been made in Chapter 6, that the boundaries of these areas are in good agreement with the origin of two different groups of cells, each projecting to a different thalamic nucleus (Orem and Schlag, 1971). Other pieces of supporting evidence exist, particularly with regard to the subdivision of the presylvian sulcus as shown in Fig. 4 of Chapter 6. Dubrovsky and Barbas (1977) have demonstrated a projection from dorsal neck muscles (e.g. biventer cervicis) to the lateral bank of the presylvian sulcus ("lateral"area). Grantyn, Grantyn, and Heuer (1975) have reported that during stimulation of the frontal lobe region corresponding to the FEF of cat as delineated in Chapter 6, neck movements could only be elicited from two zones: the lateral part of the presylvian sulcus and the lateral lower lip of the cruciate sulcus. The first area corresponds to the present "lateral" region. Furthermore, Armand and Aurenty (1977) have compared the location of cell bodies of corticospinal neurons projecting to either the cervical or lumbar levels of the spinal cord. It is of interest that the "lateral" area projects only to the cervical cord. Their data is nevertheless inconclusive, from the point

of view of head motor control, because they examined only cervical level C7 which is too posterior for consideration as a head motor region.

Unit Recording in the FEF

In cat, essentially three types of eye or head related units were found: (1) cells that discharged after the onset of saccades; (2) cells that discharged prior to EMG activity in neck muscles; and (3) cells that discharged in association with saccadic tracking.

Units of the first type were scattered within both the "medial" and "lateral" areas. These neurons exhibited a burst discharge that followed the initiation of saccades or quick phases made in either the light or dark (Table 1, item 6 and Fig. 1). These cells usually preferred an eye movement in a specific direction and this directionality was greatly enhanced during saccadic tracking (not shown). Some of these cells were activated by stimulating the biventer cervicis neck muscle. Units that received converging inputs from both neck and eye muscles were described by others in this area and it is possible that the discharge in these units is due to eye muscle proprioceptive afferents. Unit recording in monkey has also revealed cells whose discharge begins after the onset of a saccade. An example is shown in Fig. 1A (top portion) which has been taken from Bizzi (1968). A typical cat result is shown in the bottom portion of Fig. 1A. It has been argued by Bizzi that, in monkey, the post saccade discharge of this type of cell is not due to eye muscle proprioception. In cat these neurones have a special property not reported in monkey: they have strong directional preferences during visual tracking.

Units that discharged in association with and prior to neck EMG activity in the biventer cervicis neck muscle were found in the "lateral" area of the cat (Fig. 1B, bottom). All recorded EMG units could be

activated by stimulating the biventer cervicis, suggesting that they might receive neck muscle, and possibly also eye muscle proprioceptive inputs (Dubrovsky and Barbas, 1977). Furthermore, stimulation at the site where such units were recorded evoked, at low threshold, neck muscle activity. In monkey FEF, a few cells have also been reported that discharge prior to head movements. An example is shown in Fig. 1B (top portion) which was taken from Bizzi and Schiller (1970).

A number of cells were found that discharged vigorously only when the cat tracked with saccadic eye movements a visual target moving in a specific direction (Fig. 2). These cells were located primarily in the "medial" area. They did not discharge during spontaneous saccades or quick phases in the light or dark nor was their activity related to neck EMG activity in the biventer cervicis. In Fig. 2, it can be seen that the unit discharged vigorously before and during the step like sequences of saccades during upward tracking. No discharge was associated with the down phase of the tracking movement. The simplest explanation for this response is that it is visual and caused by retinal image slip during tracking. Indeed, the most common type of unit described in monkey has visual receptive fields. An example of such a unit's response is shown in Fig. 2 (part labelled "monkey") taken from Mohler, Goldberg and Wurtz (1973). It is possible that the units in cat FEF whose responses precede visual tracking are the feline equivalent. Visual fields could not be satisfactorily tested with the untrained cats used in this study. However, it is reemphasized that these units did not discharge during spontaneous saccades in the light where retinal slip did exist, although of course caused by movements of the eye itself and not by movements of the external world.

As a conclusion to this summary of the FEF experimental results, two points are emphasized. First, cells that discharge after the onset of saccades suggest a homology between the cat and monkey FEF. Second, the very characteristic modulation of cat FEF cell discharge during tracking suggests that this frontal lobe area may be implicated in the control of this behavioural task. Curiously, perseverative tracking frequently is associated with FEF lesions. However, a great deal of additional work must now be done before one can speculate usefully on FEF function.

Directions for future work

Having established the various discharge patterns found in FEF neurons, the road is now open to a more direct study of the information carried by these cells. For the units that discharge after the onset of saccades, it would be of interest to determine what aspect of their discharge is related to the saccade characteristics. For example, it appears that the duration of their burst discharge is not related to the duration of a rapid eye movement. However, their discharge frequency may be related to saccade velocity; or their discharge pattern may depend on whether it is associated with a quick phase or a saccade. With respect to this latter point, it is relevant that the results of Chapter 3 have shown no difference between quick phases and saccades. It would also be of interest to know how the burst discharge of these units relates to oblique saccades. Does the discharge code aspects of the overall movement (e.g. amplitude, direction) or does it code certain properties of one of the components? The results of Chapter 4 are relevant to these latter questions. A further question of interest is whether the discharge pattern of these cells in cat, that discharge after the onset of saccades, is determined by extraocular muscle afferents.

For the neck movement related unit activity, it would be of interest to know if these cells project to the cord (Armand and Aurenty, 1977), and to what aspect of head movement control (e.g. acceleration?) the discharge is related.

Faced with this rich store of potentially rewarding experiments, plus many others not mentioned, the author has chosen to embark initially upon a somewhat different route whose aim is to clarify the link between the FEF and the SC. The experiments reported in Chapter 8 have demonstrated an intriguing short latency response in the SC following stimulation of the FEF. Preliminary experiments have now been performed on alert behaving cats with the aim of determining the eye movement related discharge characteristics of those SC cells that are activated at short latency following FEF stimulation. It would be pleasant to end this thesis by suggesting a preliminary function for these units. However, as shown in Chapter 8, the response magnitude of these units is usually small and in chronic animals they have been difficult to hold for a period long enough to permit satisfactory testing. The experiments performed so far suggest these units do not discharge in relation to random voluntary saccades: i.e. they are not activated by CD cell discharges discussed in Chapter 7. Of course, it would be of interest to test these units during a tracking behaviour similar to the one related to the activity of the D cells of Chapter 7.

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Table 1 (Table 9-1)

Summary of the results obtained by stimulating and recording in the frontal eye field of both cat and monkey.

TABLE 1

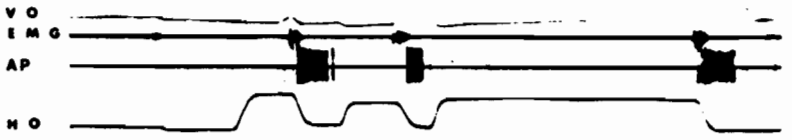
EXPERIMENTAL CONDITION	ITEM	EXPERIMENTAL RESULT	MONKEY	CAT	
				"MEDIAL" AREA	"LATERAL" AREA
SACCADES EVOKED BY STIMULATING FEF	1	Constant Amplitude & Direction of Saccades	Yes	Yes	No (Centering)
Refs. (1) Chapter 6 (2) Robinson & Fuchs, J. Neurophysiol. 32 (1969) 637-648.	2	Retinotopy	No	No	No (Centering)
	3	Topographical Rep.	No	Yes (Contralateral Saccades topographically rep.)	No (Centering)
	4	Saccade Latency	Shortest 15 msec Mean 25	Shortest 25 msec Mean 45	Shortest 40 msec Mean 60
EYE-HEAD MOVEMENT EVOKED BY STIMULATING FEF	5	Coordinated Eye-Head Movement	?	Yes	Yes (Very Low Threshold for Head Movement)
UNIT RECORDING IN FEF	6	Units Discharge after Saccades	Yes	Yes	Yes
Refs. (1) Chapter 7 (2) Bizzi,E., Exp. Br. Res. 6 (1968) 69-80. (3) Bizzi,E. & Schiller,P.H., Exp.Br.Res. 10 (1970) 151-158.	7	Units Discharge before Head	Yes	No	Yes
	8	Units have Visual Fields	Yes	?	?
	9	Units Discharge during Saccadic Pursuit	?	Yes	No
	10	Units Receive Eye and Neck Muscle Projections	?	No	Yes

Fig. 1. (Fig. 9-1)

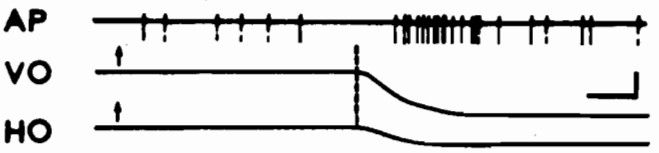
Comparison between unit discharges recorded in the FEFs of cat and monkey. A. Neurons that discharge after the onset of saccades. B. Neurons whose discharge is related to head movement (monkey) or neck EMG activity (cat). Abbreviations: VO: vertical ocular movements; HO: horizontal ocular movements; HH: horizontal head movements; EMG: EMG activity recorded in neck muscle; ∫EMG: rectified and R-C integrated EMG activity; AP: action potentials. Results for monkey obtained from: Bizzi (1968); and Bizzi and Schiller (1970).

A

MONKEY

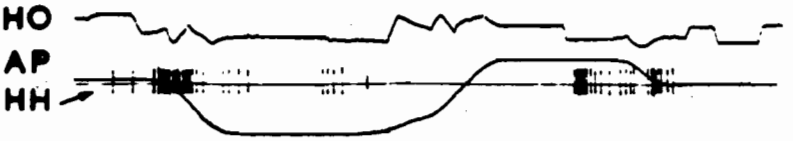


CAT



B

MONKEY



CAT

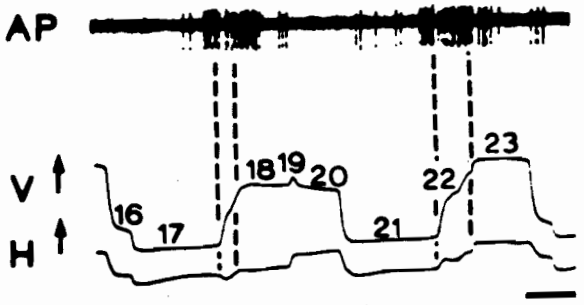
Fig. 2. (Fig. 9-2)

Unit in cat FEF whose discharge is related to ocular tracking; and unit in monkey FEF whose discharge is triggered by a visual stimulus.

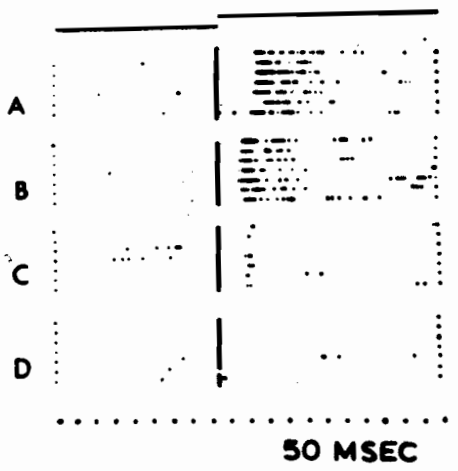
In the upper portion of this figure (CAT) the unit burst activity is related to saccade sequences directed generally upward. The animal was tracking a target and it is possible that the neuron responded to retinal image slip.

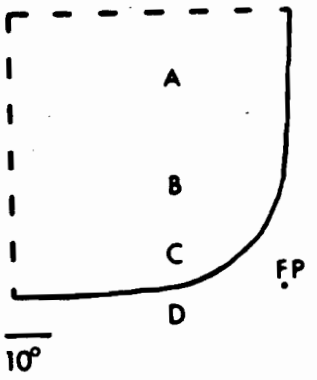
In the lower portion of this figure (MONKEY) there is shown on the left a unit's response (presented as a raster plot) to the presentation of a visual target at different positions (A, B, C) in the receptive field. The receptive field outline is shown on the right where FP is the monkey's fixation point. Note that point D lies outside the receptive field and the unit has no response. In the raster plots the onset of the light stimulus is indicated by the solid vertical lines. Results for monkey are taken from Mohler et al. (1973). Abbreviations: AP: action potentials; V and H: vertical and horizontal eye movements. Upward deflection signifies upward and rightward movements respectively.

CAT



MONKEY





CHAPTER 10

CONTRIBUTIONS TO ORIGINAL KNOWLEDGE

CONTRIBUTIONS TO ORIGINAL KNOWLEDGE

The McGill Faculty of Graduate Studies and Research requires that a Ph.D. thesis should contain a statement indicating what elements of the work are contributions to original knowledge. This chapter fulfills this obligation.

The principal contributions to knowledge are listed below.

A. Methodology

In collaboration with Mr. W. Ferch, a system that makes use of the well known eye coil in magnetic field technique, was developed to permit the precise recording of eye movements. The new instrument utilized frequency coding (as opposed, say, to phase coding) and operated at high frequency to minimize noise interference with biological signals.

B. Eye Movements of the Cat

(1) A comparison between saccades and quick phases of vestibular nystagmus has suggested that these two rapid eye movements in cat have similar temporal properties.

(2) No linear summation was found between the slow and quick phase signals of vestibular nystagmus.

(3) Oblique saccades of the cat were studied and it was shown that the duration of the horizontal and vertical components are similar. The smaller component of an oblique movement has its duration prolonged ("stretched") beyond what it would be if it existed alone as a pure horizontal or vertical movement. The temporal dependence between the orthogonal components is such that in the light the short component has its duration stretched to about 90% that of the long component. In the dark the temporal dependence is considerably weakened.

C. Stimulation of Cat Frontal Eye Field

(1) Stimulation within cat frontal lobe elicited saccadic eye movements whose maximum velocity was significantly greater than that of normal spontaneous saccades.

(2) The majority (90%) of stimulated cortical points yielded eye movements whose directions and amplitudes were independent of the position of the eye in the orbit. The direction of these eye movements depended on the site being stimulated, with a discrete and orderly representation of directions existing within the cortex.

(3) A lesser number of cortical points (10%) yielded centering movements whose directions and amplitudes depended on the position of the eye in the orbit, rather than on the site being stimulated.

(4) Evoked neck muscle activation frequently preceded evoked eye movements by some 15-30 msec. This timing was compatible with a coordinated head-eye orientating response.

(5) On the basis of the directions, and the latencies, of evoked eye movements, the cat frontal oculomotor area could be divided into two subregions, a 'medial' and a 'lateral'.

(6) The 'medial' area included the mesial wall of the hemisphere with a portion of the lower lip of the cruciate sulcus, and the medial wall of the presylvian sulcus. This area yielded contraversive eye movements with shorter latencies (average 45 msec).

(7) The 'lateral' area included primarily the lateral wall of the presylvian sulcus. It yielded predominantly centering eye movements, and ipsiversive movements with longer latencies (65 msec).

(8) The functional characteristics of the 'medial' area, as revealed by focal stimulation, resembled those of the monkey frontal eye field.

D. Unit Recording in the Cat Frontal Eye Field

(1) Cells could be grouped into three categories: (a) Units ("D" cells) that discharged before and during saccadic eye movements, whenever the eyes followed a target in one specific direction. Spontaneous saccades, or vestibularly driven nystagmus, in either the light or dark, elicited no responses. (b) Units ("CD" cells) that discharged following (i) tracking saccades; (ii) spontaneous saccades; and (iii) the quick phase of nystagmus, in all directions. There usually was a slight discharge preference for one given direction, and this preference was enhanced whenever visual tracking was restricted to the preferred direction. One-third of CD cells responded to stimulation of the contralateral biventer cervicis neck muscle (min lat. 20 msec). (c) Units ("N" cells) that discharged in association with, and preceding changes in neck muscle activity. These cells also responded to stimulation of the contralateral biventer cervicis muscle (min lat. 10 msec).

(2) For points in the "lateral" region (as defined by stimulation), the directions of evoked saccades, and the directions of spontaneous saccades associated with unit discharges, were similar. In the "medial" region, the directions of evoked saccades were roughly opposite to the directions of spontaneous eye movements favoured by unit discharges.

E. Influence of FEF Stimulation on Unit Responses in the Superior Colliculus (SC)

(1) In both the deep and intermediate layers of the SC, units were found that could be driven by FEF electrical stimulation after a latency ranging between 5-30 msec. These cells were visually unresponsive.

(2) Units were found in the intermediate layers that responded with burst discharges to both FEF and visual stimulation.

(3) In the intermediate layers some visually responsive units were found that had a subthreshold response to FEF stimulation. For these cells the influence of an FEF stimulus could be demonstrated as a distinct modification of their visually evoked responses.