Eye Movements Evoked by Stimulation of Frontal Eye Fields

D. A. ROBINSON AND A. F. FUCHS

Department of Medicine, Division of Biomedical Engineering, The Johns Hopkins School of Medicine, Baltimore, Maryland 21205

In 1874 Ferrier (4) elicited conjugate contralateral eye movements in the monkey by stimulating the cortical area now known as the frontal eye fields (Brodmann's area 8). The many subsequent studies of this phenomenon have been reviewed by Smith (22) in 1949 and Crosby, Yoss, and Henderson (3) in 1952. The usual response to electrical stimulation was a slow rotation of both eyes to the opposite side with an occasional up or down component. Other types of movements that have been observed are centering (1), vergence movements (3), and nystagmus (22). Several cortical maps showed areas on the frontal cortex where these various types of movements could be produced but there was little agreement among them. Most of these studies suffered from three limitations: 1) the animals were under light anesthesia which is known to affect the movements; 2) stimulus intensity was usually unreported, and 3) eye movements were not objectively recorded. In 1958 Krieger, Wagman, and Bender (10) reported the effects of anesthesia on cortically evoked eye movements. Although they did not record eye movements, they reported (24) that stimulation of the frontal eye fields of the unanesthetized monkey usually produced the rapid eye movements called saccades.

In 1966 we developed a method for accurately recording vertical and horizontal eye movement chronically in the monkey (6). Using it, we discovered that a brief stimulus delivered to the frontal eye fields produced a single contralateral saccadic eye movement characterized by an amplitude, a direction, a latency, and a threshold (19). Consequently, we explored the effects of cortical location on all these variables and studied the temporal interaction of evoked saccades to try to understand the role of the frontal eye fields in the control of saccadic eye movements.

METHODS

Six Macaca mulatta monkeys, each weighing 6-7 lb., were studied. Under general anesthesia they had implanted: 1) a coil of wire on one eye to measure eye movements, 2) skull bolts to immobilize the head, and 3) a chamber through which stimulating electrodes could be passed into the cortex. The eye movement recording method measures the vertical and horizontal movements of one eye, has a bandwidth of 2 kc/sec and a sensitivity of 15 min of arc (6). Three bolts were implanted in the skull, one anterior in the midline and two posterolateral over the parietal areas. The bolt heads were placed beneath the bone and their percutaneous shafts were mechanically joined above the scalp by a piece of aluminum which could be used to immobilize the animal's head. Details of this technique have been described elsewhere (7). A chamber with an inside diameter of 18 mm was implanted over each frontal eye field. The dura was left intact and the centers of the chambers were located stereotaxically (Horsley-Clarke coordinates: A, 28 mm; L, 17 mm) over the posterior tips of the principal sulci.

After a 2-day recovery period, daily recording sessions of about 4 hr. were begun and continued for from 4 to 20 days. Before each session a Teflon electrode guide was placed in the chamber which permitted the electrode track to be located anywhere in the chamber. Before the monkey was returned to its cage the electrode guide was replaced by a Teflon cap whose body completely filled the chamber so that its bottom rested on the dura. Daily aseptic procedures were used with everything that came into contact with brain tissue or the chamber interior. The monkey was supported by 160 mg/day chloramphenicol for 2 weeks and

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150,000 units of penicillin twice a week for the remainder of the experiment.

Monopolar electrodes of stainless steel or tungsten coated with Teflon (0.25 mm od) were used. They were sharpened and, directed by the Teflon guide, were thrust through the dura. Constant-current cathodal stimulation was used. Bipolar electrodes and anodal and biphasic stimulation were investigated but the results did not differ from those with monopolar cathodal stimulation. Stimulus current and both components of eye position were recorded on analogue tape and later reproduced with an overall bandwidth of 2 kc/sec. Locating pins were placed in the brain before each animal was sacrificed so that the location of any stimulated site could be reconstructed in the fixed brain.

RESULTS

Nature of evoked movements

The great majority of eye movements produced by frontal eye field stimulation were single contralateral conjugate saccades which occurred about 25 msec after the onset of stimulation. For any given electrode location the amplitude and direction of the evoked saccade was quite reproducible. The range of variability was seldom more than 15% of the mean. The amplitude and direction of the saccade was affected very little by large changes in stimulus parameters or initial eye position. A 30-msec pulse train (1 msec pulses, 200/sec) was generally used. If long pulse trains were used (e.g., 1–2 sec) a sequence or staircase of identical saccades spaced about 100 msec apart resulted which continued until the stimulus stopped or the eyes reached their mechanical limits. When the position of the electrode was changed, the threshold, amplitude, and direction also changed. Thresholds ranged from .05 ma to 2 ma, saccade amplitudes from 1 to 70°, and direction from horizontal to almost straight up or down. Centering, smooth pursuit or vergence movements or nystagmus were never observed in the awake monkey.

Saccadic nature of evoked movements. Figure 1A shows the similarity in the time course of equal-amplitude spontaneous and evoked saccades. To demonstrate that the evoked movements were in fact saccades, their durations and amplitudes were studied. There is a fixed relationship between these variables in man (8, 17, 26) and in monkey (5). The amplitude-duration relationship of spontaneous saccades for three monkeys is shown in Fig. 1B and is the same as that found by Fuchs (5) in

![Figure 1](image-url)
Macaca speciosa. Figure 1B shows that the amplitude-duration relationship of evoked movements and spontaneous saccades are in close agreement. Therefore, the evoked movements are not merely rapid or saccade-like, they are indistinguishable from the monkey's own spontaneous saccades. Neither the threshold nor the amplitude and direction of the evoked saccade was influenced by whether the eyes were open or closed (provided the animal was awake) or whether the animal had normal vision, was visually form deprived, or was in the dark.

In response to over 50,000 stimulus trains delivered to about 1,000 cortical sites, 96% of the evoked movements were single contralateral saccades. At 3.9% of all cortical sites stimulated, other responses occurred. At 3.1% of the sites, two saccades occurred. The first was always contralateral with a normal latency of about 25 msec. The second was either ipsilateral (1.9%) or contralateral (1.2%) and followed the first after 50-200 msec. At 0.6% of the cortical sites, stimulation produced movements that seemed to be composed of two saccades back to back, the first contralateral followed immediately by a smaller ipsilateral saccade. At 0.2% of the sites, single ipsilateral saccades were evoked. All of the responses were therefore saccadic in nature, and the small percentage of anomalous responses should not draw attention away from the fact that the great majority of responses to stimulation of the frontal eye fields were single contralateral saccades. It should also be emphasized that the failure to observe nonsaccadic movements (such as smooth and vergence movements and nystagmus) is based on a large number of observations and a large variety of stimulus conditions.

STIMULUS PARAMETERS. The evoked saccade exhibited an all-or-nothing behavior. There was no response below a certain current value, and, above it, the size and direction of the evoked saccade varied little with current strength. The threshold varied from moment to moment over a 2:1 range so that as the current was increased from below, the probability of evoking a saccade grew from 0 to 1; however, whenever a movement did occur, its amplitude and direction were constant. Threshold was defined as the least current required to evoke a movement for every stimulus.

With a train of 1-msec pulses at 200/sec, the train length was varied at 13 locations. A typical latency was 25 msec and a typical saccade duration was 25 msec, so that stimulation beyond 50 msec could no longer influence the saccade. The saccade amplitude began to decrease when the train length was 35 msec and dropped by 60% at 20 msec; at shorter train lengths the stimulus went below threshold. The direction of the saccade did not change. If the train length was held constant at, say, 50 msec and the stimulus current was increased, the amplitude of the saccade did not change until the current was about three times threshold. Above this the amplitude decreased slowly, reaching half its former value for very strong currents. The latency decreased from 25 msec at threshold to as little as 15 msec for strong stimuli, and a saccade with an initial up or down slant became more horizontal.

If the current amplitude and train length were held constant, variation of the pulse width (0.5-4 msec) and repetition rate (100-1,000/sec) had no effect on threshold or the saccade. When the pulse rate became very small, the oculomotor system began to react to each pulse in the train rather than to the train as a whole. Livingston (11) used 10-msec pulses in the frontal eye fields of the anesthetized monkey and reported that the evoked eye movements could be changed from contralateral to ipsilateral by lowering the stimulus rate from 30-60/sec to 1-13/sec. In trying to repeat this observation in the alert animal we found that a stimulus rate of 1-13/sec merely produced contralateral saccades at 1-13/sec.

In summary, all the stimulus parameters could be varied over wide ranges without affecting saccade size or direction. Consequently our impression is that the amplitude and direction of an evoked saccade depended much more on where the cortex was stimulated than on how it was stimulated.

INITIAL POSITION. The amplitude and direction of the evoked saccade varied only slightly with the initial position of the eye. For example, if a cortical site produced a
10° contralateral horizontal saccade with the eye in the primary position, the amplitude might be 13° if the monkey were looking ipsilaterally and only 8° if it were looking contralaterally at the time of stimulation. If the eyes were initially elevated the movement might have a downward slant of 15° or, if depressed, an upward slant of 15°. Our general conclusion is that the direction and amplitude of the evoked saccades were relatively independent of eye position at the moment of stimulation and moved in the same direction and by the same amount (depending on cortical location) when stimulated. This behavior is quite different from goal-directed (9) movements in which stimulation causes the eyes to move to the same final position from any initial point.

EFFECTS OF ANESTHESIA. Krieger and associates (10) investigated the effects of thiopental sodium on cortically evoked eye movements in the monkey and found, with increasing dose: 1) spontaneous, low-amplitude, rapid nystagmus; 2) contralateral nystagmus on stimulation; 3) a loss of vertical components in the evoked movements; 4) a decrease in the area of excitable cortex; 5) a decrease in the speed of the evoked movements; 6) an increase in the number of sites producing centering movements; and 7) disconjugate movements. We share their opinion that many of the contradictory results of previous work came from the use of anesthesia. A study of three cortical sites in one monkey under the effect of 6.8 and 13.6 mg/kg of sodium pentobarbital confirmed all but the first of their observations (probably due to the different anesthetic agent).

When the lighter dose was administered intravenously, the animal made disorganized limb movements and saccades in response to a loud noise, and two additional phenomena were observed. 1) There was a total loss of smooth pursuit eye movements which are compellingly induced in an awake animal by rotating a large mirror before it. A similar observation has been made in man (16). 2) Spontaneous saccades in any direction were slower than normal and were followed at once by a slow, exponential return to the primary position.

Evidently, the ability to maintain fixation was also lost, and the passive orbital tissues were free to pull the globe back to the center. Therefore, when the cortex was stimulated by a long train, the evoked saccades moved the eyes contralaterally in quick phases interspersed with slow returning movements. This gives the appearance of nystagmus, two beats of which are shown in Fig. 2B, and we believe that this is the phenomenon observed by Krieger et al. (10) and by Smith (22). It probably should not be called nystagmus because it has a simple mechanical explanation and is unrelated to the neurogenic activity of optokinetic or vestibular nystagmus. Stimulation produced saccades much like the slowed spontaneous saccades at this anesthetic level. The latency increased and became variable (30–100 msec), the velocity of the movements decreased and their duration increased.

When the animal rested quietly at the anesthetic level of 6.8 mg/kg, it sank to a depressed state which abolished all saccades, either spontaneous or evoked. Stimulation by a long train produced the slow smooth movement shown in Fig. 2C. This state abolished all responses for current

![Figure 2. Effect of sodium pentobarbital on eye movements evoked by frontal eye field stimulation. Stimulus was 0.3 ma, 1-msec pulses at 200/sec. Train length is indicated by heavy lines. A: no anesthesia. B: 6.8 mg/kg administered with animal aroused by loud noises (note nystagmoid appearance). C: same dose level as before but with animal allowed to sink to a more depressed state. D: lack of response at 13.6 mg/kg at 1.0 ma.](image-url)
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strengths up to 2 ma at one cortical site, yielded only smooth movements at a higher threshold (up by 1.6) at a second site, and either smooth movements or degraded saccades at the preanesthetic threshold at the third site. Thus, in general, larger currents were needed to produce a movement. It has already been reported that as stimulus current increased, the evoked movements became more horizontal in the awake animal. This is probably also the case with anesthesia and may account for the third finding of Krieger and co-workers (10).

When the anesthetic dose was doubled, the animal’s eyes closed, all spontaneous eye movements ceased except for a slow random drifting, and stimulation at previous intensities produced no eye movements. When the current was increased to about 7 ma, slow centering movements were observed at three different cortical sites. A current strength of 7 ma is very large and, according to the work of Phillips (15), probably excites cells and axons as far as 15 mm from the electrode tip. Movements elicited by such large currents are difficult to relate to cortical localization. At this depth of narcosis we also observed disjunctive movements.

Thus we confirmed the observations of Krieger et al. (10) and can add to them: 1a) the early total loss of smooth pursuit movements, and 1b) a concomitant loss of the ability to maintain fixation. In summary, smooth pursuit, vergence and centering movements, and nystagmus may all be produced by the combination of anesthesia and the large stimulus currents its use necessitates.

Stimulus location

In four animals at least one frontal eye field was thoroughly mapped by recording the threshold, amplitude, and direction of the saccades evoked at over 300 locations. Figure 3 shows a typical map. In and near gray matter in the sensitive region between the principal and arcuate sulci, thresholds lay between 0.1 and 0.5 ma as shown by the isothreshold contours in Fig. 3. Stimulus currents greater than 2 ma were not used because current spread would excite a very large radius of tissue (estimated at 7 mm).

Although some variability was seen in the four monkeys studied, four cortical regions emerged with certain constant features from one animal to another (Fig. 3D). They were: 1) a region anterior to the posterior angle of the arcuate sulcus where stimulation produced small (1-5°) more or less horizontal saccades; 2) a region between the superior limb of the arcuate sulcus and the posterior tip of the principal sulcus where medium-sized horizontal saccades (5-15°) were evoked; 3) a small spot (3-4 mm in diameter) in the buried cortex within region 2 where stimulation produced saccades with large up or down components; and 4) a broad region anterior to region 2 under the upper ramus of the arcuate sulcus where the threshold was high (1-2 ma) and the evoked saccades were large (20-60°), horizontal, and of long latency (50-100 msec). There was considerable variability in the location and shape of the principal and arcuate sulci between hemispheres and from one animal to another which extended to the location of the four regions with respect to these landmarks. The size of an evoked saccade seldom changed radically from one cortical point to another nearby. The transition from small to medium to large saccades was generally a gradual one. In contrast to other workers, notably Crosby et al. (3), we found that stimulating the cortex between the principal sulcus and the inferior limb of the arcuate sulcus did not produce eye movements (at currents below 2 ma) in any of the six animals.

Although regions 1, 2, and 4 produced primarily horizontal movements, it was not unusual to find movements tilted up or down by 30 or even 45°. In region 3, however, the movements were typically tilted 60 or 75° up or down. They were 10-20° in amplitude, and small displacements of the electrode tip often produced a large change in the amount and direction of tilt. The cortex pictured in Fig. 3A shows the low-threshold area extending superiorly to the limit of the chamber. This was not typical and in the other three animals the area excited by 1.0 ma or less did not extend superiorly beyond the arcuate sulcus. In region 4 it was necessary to use stimulus trains as long as 100 msec to evoke a sac-
The evoked saccades were large, with 20–30° being usual and 60–70° seen occasionally.

**Temporal interaction**

Since a saccade evoked by frontal eye field stimulation is an all-or-nothing phenomenon with a threshold, and therefore quite different from movements produced by stimulation of other motor areas in the cortex, one may ask if, like other pulsatile phenomena, the saccade is followed by a relative and absolute refractory period.

**Double pulse-train stimulation.** Refractoriness could be demonstrated when a threshold-conditioning pulse train was followed $T$ milliseconds later by a test pulse train. Figure 4 shows results typical of the 21 sites tested. As $T$ decreased from 200 msec, the second response became smaller and its threshold increased. At 50 msec, the second response could not be elicited. The means of the absolute and relative refractory periods at the 21 sites were 49 msec ($\pm 20$ sd; range 25–100 msec) and 42 msec ($\pm 18$ sd; range 10–75 msec), respectively. Although the amplitude of the second movement de-
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Fig. 4. Demonstration of absolute and relative refractoriness. A conditioning train of intensity $I_1$ was followed by a test train $I_2$ after $T$ milliseconds. Stimulus trains are indicated by heavy bars. Right cortex was stimulated evoking horizontal saccades to the left (down) about 18° in amplitude. Threshold stimulus $I_0$, and amplitude of the second saccade expressed as a fraction of the first are indicated near the second response.

creased during the relative refractory period, its direction did not change.

UNILATERAL TWO-POINT STIMULATION. In this series a threshold-conditioning stimulus, $I_1$, was delivered to one point and the test stimulus, $I_2$, was delivered $T$ milliseconds later to another point in the frontal eye field on the same side. The distance between point pairs ranged from 3.2 to 6 mm. There were two questions asked in these experiments: 1) was there a refractory period and 2) if the saccades evoked from the two sites had different amplitudes and directions, what would happen when the sites were stimulated simultaneously? All nine point pairs tested gave similar results. A typical example is shown in Fig. 5A. Relative refractoriness began when $T$ was 100 msec with a drop in the amplitude of the second movement. As $T$ decreased to 37.5 msec the second movement became quite small and its threshold rose to 0.8 ma. The mean relative refractory period (between stimuli) was 59 msec (range 20–100 msec) and the mean absolute refractory period was 59 msec (range 30–100 msec) for the nine point pairs. These figures are not considered different from the results of double stimulation at a single point. The direction of the second movement did not change during the relative refractory period, and both horizontal and vertical components diminished together.

When both points were stimulated simultaneously, the size and direction of the resultant movement lost its all-or-nothing character and could be graded between the movements produced by stimulating each point singly by altering the relative amplitudes of the stimulus currents $I_1$ and $I_2$. Figure 5B illustrates this grading for a site pair chosen to have opposite vertical components. The amplitude and direction of each saccade is represented by a vector. The threshold value of $I_1$ by itself was 0.3 ma, but when $I_2$ was only 0.08 ma, it affected the amplitude and direction of the saccade evoked by $I_1$. As $I_1$ increased to 0.3 ma it finally dominated the movement entirely. The response when $I_1$ was 0.3 ma was the same whether $I_2$ was present or not. At some combination of $I_1$ and $I_2$ the movement could be put about halfway between the two responses elicited singly (e.g., Fig. 5B, $I_9 = 0.4, I_1 = 0.08$ ma). If $I_1$ were increased so that the size and direction of the movement changed, it could be restored by a subsequent increase in $I_2$.

Figure 5B illustrates the following features found at all homolateral point pairs investigated. 1) A stimulus current could begin affecting the resultant movement at an intensity well below its threshold value. 2) When both stimuli were used at threshold, the movement was seldom balanced and one stimulus usually dominated. 3) The resultant movement was not the vector sum of the two individual movements, but a weighted vector sum in which the weighting factors were functions of the ratio $I_1/I_2$. 4) The amplitude of the movement clearly is not a function of how many corticofugal fibers are excited since, in Fig. 5B, an increase in $I_1$ from 0 to 0.08 ma...
FIG. 5. Temporal and spatial interactions of saccades evoked by stimulating two different cortical sites on same hemisphere. A: demonstration of refractoriness. A conditioning train of intensity I₁ at one site was followed by a test train I₂ after T milliseconds at another. Left cortex was stimulated evoking rightward (up) horizontal saccades. First evoked saccade was about 15°, the second about 12°. Threshold value I₁ and amplitude of the second saccade expressed as a fraction of its value when it occurred alone are shown near the second saccade. B: grading of saccade size and direction for a different pair of sites on right cortex. Saccades are shown as vectors in a frontal view. U, D, L, R are up, down, left and right. T was zero, I₁ and I₂ thresholds were 0.3 and 0.4 ma, respectively. Response to I₁ was a 20° saccade down to the left, to I₂, 6° up to the left. As I₁ increased from 0 to 0.3 ma the size and direction of the movement changed smoothly.

caused a decrease in the amplitude of the movement.

BILATERAL TWO-POINT STIMULATION. As early as 1890, Mott and Schaefer (14) demonstrated that bilateral stimulation could lead to cancellation of the movements evoked from each frontal eye field. Since these movements are saccades in the awake animal, one may inquire, as before, whether a refractory period is demonstrable, and how the amplitude and direction of the net movement is determined for simultaneous stimulation. All 19 point pairs studied gave results similar to those shown in Fig. 6A. A threshold-conditioning stimulus on the right cortex did not create a refractory period for a test stimulus on the left, and the second saccade retained its full amplitude until the two movements began to overlap in time when T was 30 msec. When T was 20 msec, the movements interfered in such a way that the first appeared to be canceled (in midflight) and replaced by all or a fraction of the second. This fraction could be graded from zero to full size by varying I₂. When T was zero, a single saccade down to the left, to I₁, 6° up to the left. As I₁ increased from 0 to 0.3 ma the size and direction of the movement changed smoothly.

Figure 6B shows the responses of another point pair in vector form which produced movements with up and down components and illustrates how changing the intensities I₁ and I₂ shifted the net movement anywhere between the two produced by either I₁ or I₂ alone. At one ratio of currents the vertical components canceled producing a horizontal saccade; at another, the horizontal components canceled producing a vertical saccade. It was of interest to see if the small residual movements, when the two stimuli almost canceled, were, in fact,
saccades. Consequently, for one pair of points which produced large (15–20°) horizontal movements, the durations of the small net saccades produced by simultaneous stimulation were measured. They were found to lie on the amplitude-duration curve shown in Fig. 1B, indicating that they were saccades. Specifically, although \( I_1 \) and \( I_2 \) separately produced saccades whose durations were 38 msec, when they acted together and produced, say, a 5° saccade, its duration was only 23 msec.

Although there was no refractoriness to the horizontal components of saccades, Fig. 6C illustrates that if a saccade with an up component was elicited from one side, a relative and absolute refractory period could be demonstrated to the up component of a movement evoked from the opposite side. Of the 19 point pairs tested, only 12 had vertical components in both movements. Of these, 4 had vertical components in opposite directions and did not display refractoriness. The other 8 had vertical components in the same direction. Of these, all 8 showed relative refractoriness commencing at a mean delay \( T \) of 66 msec (range 25–100 msec), and 5 showed absolute refractoriness at a mean delay of 38 msec (range 30–50 msec).

A summary of the results of temporal interaction can best be given by an example. If the left frontal eye field were stimulated and produced a saccade down and to the right, the oculomotor system would be refractory to a saccade with another right horizontal component evoked from either side but not a left horizontal component evoked from stimulation of the right frontal eye field. Similarly, the down
component of a second saccade during this period could not be evoked by stimulation of either side, but an up component of a second saccade could be evoked from the right cortex but not the left. Put another way, saccades with horizontal and vertical components in the same direction as the conditioning saccade cannot be evoked during the refractory period by stimulating anywhere in either frontal eye field, but a saccade with opposite components can be evoked by stimulation of the opposite frontal eye field.

**DISCUSSION**

The proposition that stimulation of the frontal eye fields in the awake monkey produces conjugate saccadic eye movements seems a likely one since it is based, in these experiments, on a great many observations. It is strengthened by the fact that nonsaccadic movements such as smooth, vergence and centering movements, and nystagmus are never observed in the awake animal, and can only be produced by the use of anesthesia and large stimulus currents. The implication is that, had anesthesia not been used in previous studies, nonsaccadic movements might not have been observed.

Stimulation has suggested a premotor function for the frontal eye fields and the short latency we observed between stimulus and eye movement strengthens this idea. The latency was usually 25 msec, but strong stimulation shortened this to 15 msec. Since a 5-msec latency exists between third nerve stimulation and eye movement (18), the fastest connections from the cortex to the motor nuclei require 10 msec. This suggests that, whereas fibers descending from the frontal eye fields do not synapse directly on motoneurons (a connection also precluded by the all-or-nothing nature of the response, and supported by anatomical studies (3)), they are at least closely coupled to the motor nuclei.

Based not only on stimulation results but eye movement disturbances in man involving frontal lobe lesions, it has long been thought that the frontal eye fields were somehow concerned with voluntary saccades. The fact that saccades of different amplitudes can be reliably evoked from different regions within the frontal eye fields implies some difference of function between these regions. There is a temptation to hypothesize a localization in the frontal eye fields for every possible size and direction of saccade that the animal needs to make. This simple view is not likely to be correct because of the unnatural nature of electrical stimulation and especially because of the single-unit study of this area by Bizzi (2). He found single units whose activity was related to eye movement, but none of them changed their discharge rate prior to a saccadic movement, which raises the question of whether the frontal eye fields are in a motor pathway at all.

Stimulation of other cortical motor areas produces limb movements whose amplitude and duration can be altered by stimulus intensity and duration. The situation is quite different when the frontal eye fields are stimulated, for the amplitude, duration, and direction of the movement are independent of the stimulus so long as it is above threshold. It would appear that the stimulus sets in motion a train of autonomous events which run their course independent of concurrent stimulus behavior. There are many examples in living and nonliving systems of such pulsatile elements (e.g., the nerve action potential). They have, in common, the properties of a threshold, an all-or-nothing response, and an absolute and a relative refractory period. We suggest that there are neuronal circuits in the brain stem which behave in this same pulsatile manner and produce the burst of activity seen to accompany saccades.

During a saccade, motoneurons of the agonist muscles discharge at rates as high as 200-400/sec (21, 25) and many neurons, previously silent, are recruited into the active pool at equally high rates. At the end of a saccade many units cease firing and others lower their discharge rates to much smaller values associated with holding the eye in the new position. During a saccade, motoneurons of the antagonist muscle are totally inhibited (21). This burst of activity (or inhibition) is reflected in the electromyogram (13, 23) and the isometric tension of extraocular muscles recorded either in the intact eye (17) or from a single muscle detached from the globe during strabismus surgery (20). It is thus well
established that saccades are produced by a burst of neural activity that is reciprocally distributed to the agonist and antagonist pairs of yoke muscles. The responsible neural circuits are probably located in the brain stem between the levels of the IIIrd and VIIth nuclei (12).

We feel that the refractoriness observed in these experiments did not arise in the cortex of the frontal eye fields for two reasons. In most of the experiments corticofugal fibers were stimulated directly which would bypass influences from the more distal cortical gray matter. Second, stimulation of one cortex that produced a saccade with an up (or down) component set up a refractory interval that blocked the up (or down) component of a saccade produced by contralateral stimulation. Consequently, it seems reasonable to suppose that the refractoriness is the property of the pulsatile brain-stem circuits themselves. Since there is no refractoriness for horizontal components when the test stimulus is delivered to the contralateral frontal eye field, it seems unlikely that a single pulsatile circuit can be responsible for producing saccades to both left and right. It is more likely that there are two such pulse generators, appropriately connected to the musculature so that one produces leftward and the other rightward saccades. A pulse of activity in one circuit would then produce a refractory condition in itself but not in the other.

Both vertical and horizontal components of a saccade conform to the amplitude-duration relationship shown in Fig. 1B. This means that when a saccade occurs with a large horizontal component and a small vertical component, the two components may start together, but they do not stop together. This precludes the possibility that they were produced by the same pulse. Therefore, two more neural circuits may exist which produce up and down saccades. A pulse of activity in one circuit would then produce a refractory condition in itself but not in the other.

The finding that saccade amplitude and direction could be graded by changing stimulus strengths when two points in the frontal eye fields are excited simultaneously is surprising. Since the movement produced by stimulation of one site is an all-or-nothing phenomenon, one might expect the all-or-nothing nature to persist when two sites are stimulated; that is, the evoked movement would be that produced from one site or the other but would never be anything in between. Since a saccade is the product of a nearly maximum effort on the part of the muscles and motor nuclei, larger saccades are produced, not by more force but by a longer saccade duration, as shown in Fig. 1B. But saccade duration is equal to the duration of the pulse of brain-stem activity so that saccade amplitude has its genesis in whatever neural networks have control over pulse duration. Since frontal eye field stimulation can produce saccades whose amplitudes differ from one location to another over a 70:1 range, the stimulation must clearly have some way not only of triggering the pulsatile circuits but of doing so in a way by which pulse duration can be affected over a wide range (3:1 as estimated by Fig. 1B). The pulse width is determined not by how many fibers are excited (since saccade amplitude is independent of stimulus current above threshold) but which fibers are excited. This is emphasized in Fig. 5B where stimulating more fibers (by increasing I1) actually decreased the saccade amplitude. Apparently the networks which control pulse width are influenced differently by descending volleys from different regions within the frontal eye fields and when two volleys reach it simultaneously (from either frontal eye field) it somehow strikes a compromise between them and produces a pulse width intermediate between the pulse widths associated with each volley separately.

The hypotheses based on the temporal interactions of evoked saccades offer interesting areas for further speculation and experiments. For the temporal interaction studies the frontal eye fields serve only as a region from which saccades can be evoked, and the resulting inferences on brain stem
organization do not, unfortunately, throw much light on the function of those eye fields themselves.

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Present address of A. F. Fuchs: Regional Primate Research Center, University of Washington, Seattle, Wash. 98105.