strated by our observation that, in a 15°C environment, periods of paradoxical sleep are not accompanied by rises in blood and brain temperatures. At this ambient temperature, although the rabbit is able to maintain a normal deep blood temperature (38.5° to 39.0°C), its cutaneous vessels are fully constricted so that the ear temperature remains near the ambient temperature. Thus, since the vessels of the skin of the ear are constricted maximally in response to the environmental thermal stimulus, there can be no further vasoconstriction during paradoxical sleep.

The experiments which we conducted at high ambient temperatures are perhaps the most interesting, pointing as they do to a disturbance in thermoregulation during paradoxical sleep. At an ambient temperature of 32°C, the rabbit, which can neither sweat nor pant effectively, is under severe thermal stress, its blood and brain temperatures elevated as much as 1°C. The skin of the ear is "clamped" in vasodilatation, allowing maximum heat loss, and even the usual small changes in temperature are absent; yet, in the face of hyperthermia, the skin of the ear shows a paradoxical vasoconstriction during paradoxical sleep, raising the central temperatures still higher. Thus these autonomic thermal correlates of paradoxical sleep in the rabbit are very persistent, superseding the thermoregulatory needs in a hot environment. This is clearly a disruption in the normal control of autonomic outflow. If the lower brainstem regions which have been postulated as necessary for the occurrence of paradoxical sleep (*3*) are initiating these autonomic events, the effect might be mediated through ascending influences on the preoptic-anterior hypothalamic region by activation of thermoregulatory neurons or through a change in the temperature "set point" (*10*). Alternatively, this autonomic response might represent an interference with descending thermoregulatory pathways, rhombencephalic regions acting more directly on preganglionic sympathetic effector neurons in the spinal cord. Other evidence of activity in the autonomic sphere during paradoxical sleep, such as lowered arterial blood pressure, irregularities in heart and respiratory rates, and changes in galvanic skin response and in pupillomotor control have been described (*3*).

Our studies confirm earlier reports (*2*) of 0.1° to 0.4°C elevations in brain temperature in paradoxical sleep, and our work shows that these elevations are due to a rise in the temperature of the cerebral arterial blood consequent to a vasoconstriction in the skin and a decrease in peripheral heat loss (*9*). Though our present thermal technique, which can be used to demonstrate large changes in heat production and blood flow in the brain (*5*), did not disclose such local events during paradoxical sleep, future studies using more sensitive temperature measurements may uncover such changes (*4*). The striking peripheral vasomotor activity which invariably accompanies paradoxical sleep in the rabbit suggests that further studies of vegetative phenomena might elucidate the role of the autonomic nervous system in paradoxical sleep.

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Discharge of Frontal Eye Field Neurons during Eye Movements in Unanesthetized Monkeys

Abstract. *Single unit activity was recorded from the frontal eye fields (area 8) in unanesthetized monkeys seated in a primate chair with the head restrained. The frontal eye field units were identified by antidromic response to stimulation of the cerebral peduncle. The findings indicate that most of the neurons discharge only after initiation of eye movements. These cells showed steady discharge when the eyes were immobile and oriented in a specific direction.*

The cerebral cortex of man and lower primates contains large regions concerned with eye movement. Among these is an area called the frontal eye field (usually homologized with area 8 of Brodmann), which lies in the frontal lobe along the anterior border of the arcuate fissure. Electrical stimulation applied to different points in the region evokes conjugate horizontal or vertical eye movement in primates (*1*). The importance of the area for the control of eye movement has further been seen in experiments involving lesions in both monkeys and man (*2, 3*). In spite of the fact that the reported effects of these lesions vary from a complete loss of voluntary eye movement (*2*) to a transient paresis of gaze (*4*), there is little doubt that subtle but lasting deficits of certain oculomotor functions occur following extirpation of the area (*3*). It has been found, for instance, that patients with lesions involving the frontal lobes show a prolongation of visual search time when required to use active head and eye movements in matching patterns (*3*).

While the methods of electrical stimulation and ablation which have thus far been employed in studies of the

frontal eye field have been valuable in outlining a region of the frontal lobes specifically concerned with oculomotor functions, these approaches do not give any indication as to the timing of discharge of frontal eye field neurons during eye movement. In the experiment reported here a recently developed method of recording single unit activity in unrestrained animals (*5*) has been utilized to investigate whether the neurons of the frontal eye field discharged immediately before an eye movement, during the movement itself, or in relation to a specific direction of gaze. The findings indicate that (i) the majority of neurons in the frontal eye fields discharge in relation to eye position, and (ii) in general the units in this area discharge only after the initiation of eye movement.

The activity of single frontal eye field neurons was recorded by means of a hydraulic microelectrode positioner (*5*), carrying a platinum microelectrode insulated by glass. Electrodes for recording the activity of eye muscles were permanently implanted between the lateral rectus and Tenon's capsule. Stimulating electrodes were placed in the cerebral peduncle. Vertical and horizontal eye movements were recorded with silver–silver chloride electrodes attached around the orbit. During the recording session, the monkey was seated in a primate chair with head restrained (*6*), and the microelectrode was lowered into the region of the frontal eye field. After a unit was found, brief electrical pulses were delivered by means of the peduncle electrodes to the fibers of the cortico-bulbar tract, which is known to receive some of the efferent pathways from the frontal eye field (*1*). Thus, some of the neurons of the frontal eye field sending axons to the brainstem via the cortico-bulbar tract could be identified by the occurrence of an antidromic response. Potentials were considered to be antidromically generated if the latency from the stimulus was invariable and if the unit responded to high-frequency stimulation (100 per second). In a series of three monkeys 300 frontal eye field neurons were recorded. For each unit the discharge pattern was observed during voluntary eye movement. Only one-third of these neurons had a pattern of discharge clearly related to eye movement, and of these 100 units, only 40 were antidromically activated. This report is primarily concerned with units of the latter type, that is, with units which were both antidromically activated and related to eye position.

The great majority of antidromically activated frontal eye field neurons (37 out of 40) showed a maximum discharge frequency for a specific direction of gaze. Figure 1, A and B, shows a frontal eye field cell which discharged steadily when the eyes were turned to the right. This figure also shows that deviations in eye position are associated with changes in unitary discharge. The discharge frequency corresponding to a particular eye position began after the initiation of the eye movement, sometimes reaching its steady rate as the eye was approaching this position and at other times reaching this rate only after the position had been assumed (Fig. 1, A and B). Units showed little adaptation during prolonged fixation (Fig. 1A). No "on" bursts characterized the beginning of this steady discharge, and no "off" bursts characterized its termination. Figure 2 illustrates that the frequency of discharge reached by a frontal eye field neuron for a given eye position was not dependent upon the direction from which this position was approached. Discharge did not occur when the eye passed through a position which would have been associated with neuronal activity had the eye come to rest in this position (Fig. 1C).

Of the 100 units which were related to eye movement, 60 were not antidromically activated. Of these 60 units, the majority showed a pattern of discharge indistinguishable from that of the antidromically activated units. A few units of this group, however, displayed a more phasic type of activity which began after the initiation of an eye movement and lasted for a very

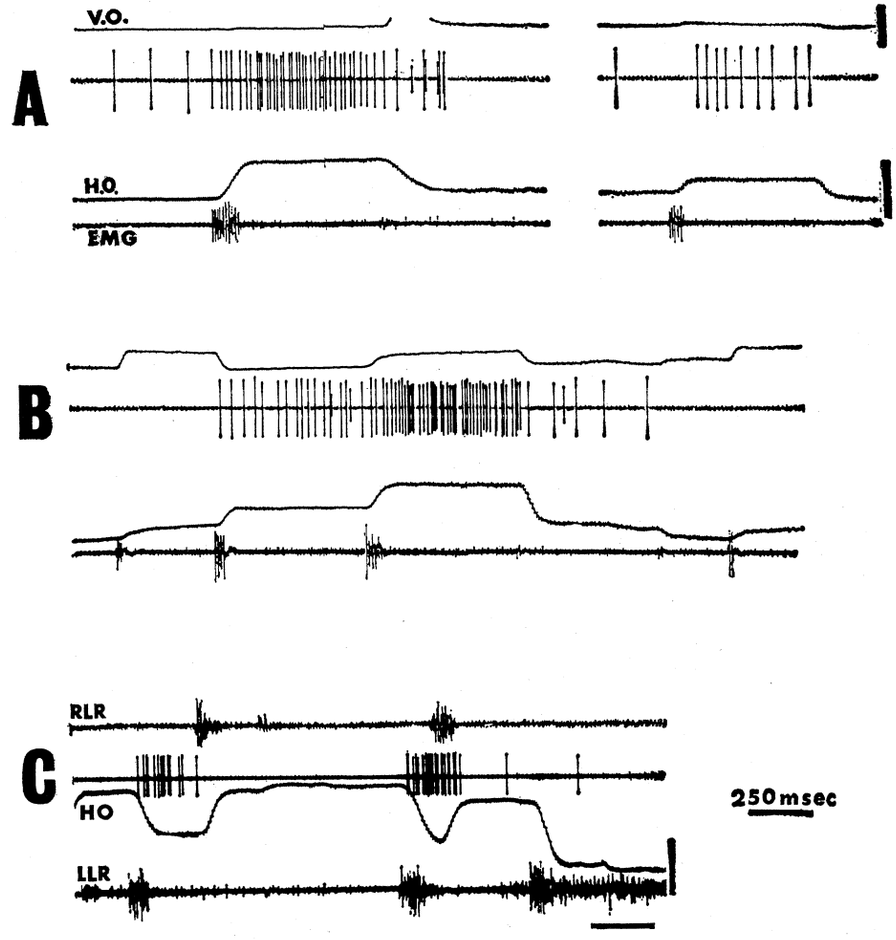

Fig. 1. Discharge of single antidromically activated units (A, B, C) recorded in different experiments from the frontal eye fields during eye movement. *V.O.*, vertical oculogram; *H.O.*, horizontal oculogram. Electromiographic record (*EMG*) from lateral rectus muscle on the right (*RLR*) and left (*LLR*) side. Vertical bars indicate 20° and 10° when related to *H.O.* and *V.O.*

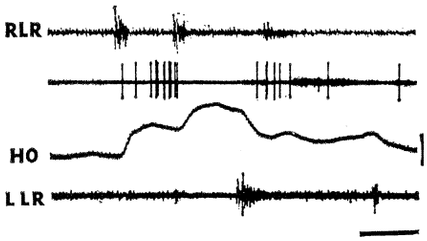

Fig. 2. Discharges of single units recorded from the frontal eye field. *H.O.*, horizontal oculogram and electromiogram record from lateral rectus on the right side (*RLR*) and from the left side (*LLR*). Vertical bar, 20°; time calibration, 200 msec.

short time at the beginning of fixation (Fig. 3B, left column). During caloric nystagmus, units belonging to this group showed clear and regular discharges in relation to the fast phase of the nystagmus (Fig. 3B, right column). This finding indicates that inputs from either the vestibular nuclei or from the eye-muscle proprioceptors reach the frontal eye field and selectively discharge certain types of neurons there (Fig. 3B). In contrast, the activity of the antidromically activated units was rarely, if at all, modified during caloric nystagmus (Fig. 3A, right column).

Two main findings have emerged from this investigation of frontal eye field neurons. First, neurons related to eye position showed a change in activity only after initiation of eye movements; second, the great majority of cells identified by antidromic responses showed steady discharge when the eyes were immobile and oriented in a specific direction.

The fact that neurons discharging prior to an eye movement have not been found suggests that the frontal eye fields are not involved, at least in any conspicuous way, in the events leading to the initiation of a voluntary eye movement. This finding is in agreement with the observation that ablation of area 8 produces paralysis lasting only a few days, followed by complete recovery of eye mobility, turning of the eyes, fixation, and optokinetic nystagmus being described as normal (*4*).

The relation of frontal eye field neurons to eye movements is thus different from the relation of precentral motor-cortex neurons to hand movements: neurons in the motor area related to the hand commonly discharge prior to the initiation of movement (*7*), and the ablation of this area results in lasting motor deficits. In contrast, frontal eye field units which discharge at the end of an ocular movement appear to be related to the effect of movement, thereby permitting two possible interpretations which are not mutually exclusive: (i) the units may be involved in tonic control of the particular postures assumed by the eye, and (ii) these cells might enter into the preparation of those postural adjustments which are necessary for the coordination of head and eyes and for the initiation of control of visually guided reaching movements. Both of these interpretations are speculative, but each suggests and requires a number of specific tests. Under the first assumption, the efferent discharges of the frontal eye field neurons, with axons terminating in the superior colliculus and in the reticular formation (*8*), might act upon the mesopontine oculomotor centers. There, the frontal eye field output might play a role in controlling the tonic aspects of eye-muscle contraction during fixation, or, alternatively, might modify some aspect of the fine eye movements which persist even during fixation (microsaccades) (*9*). If this interpretation were correct, one should find that the fine oscillatory eye tremor would be modified (presumably accentuated) after removal of the frontal eye fields.

The second interpretation of frontal eye field activity goes further by assuming that these units are involved in those complex coordinations whereby orienting and reaching movements are adjusted to each other in such a way that shifts of gaze are followed by appropriate head and limb movements. Consistent with this view are observations on man with frontal lesions leading to certain characteristic difficulties of visuomotor performance, such as difficulties in gauging the visual vertical under conditions of body tilt (*10*), and more recent observations on monkeys with frontal lobectomies (*11*) showing a specific failure to adapt their visuomotor performance to the presence of distorting prismatic spectacles. However, neither the experiments in man nor those on monkeys have been done with lesions confined to the frontal eye fields.

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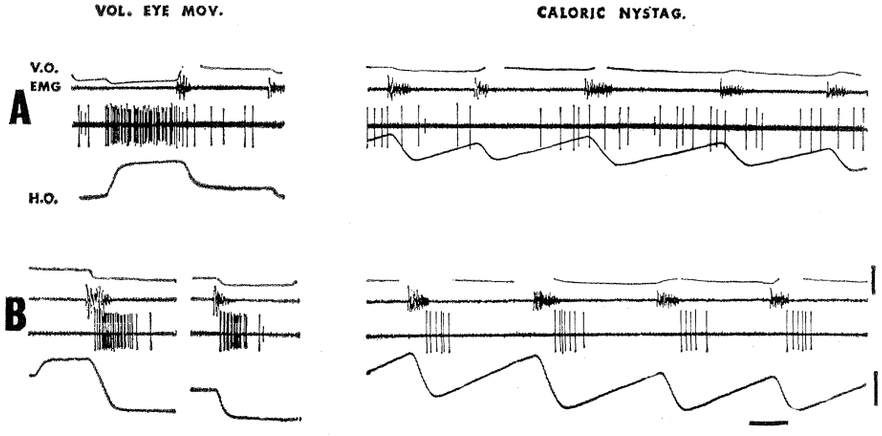

Fig. 3. (A) Discharge of a single frontal eye field unit (antidromically activated) during voluntary eye movement (left column) and during caloric irrigation of left ear (right column). (B) Discharge of a single frontal eye field unit (not antidromically activated during voluntary movement and caloric irrigation of the left ear. *V.O.*, vertical oculogram; *H.O.*, horizontal oculogram; vertical bar, 20°; time calibration, 250 msec.

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