

Convergence, Divergence, Pupillary Reactions and Accommodation of the Eyes from Faradic Stimulation of the Macaque Brain^{1,2}

ROBERT S. JAMPEL³

Laboratory of Comparative Neurology of the Department of Anatomy and Department of Ophthalmology, University of Michigan, Ann Arbor, Michigan

The neuroanatomical pathways involved in eye movements and in the control of the intrinsic eye muscles are of widespread clinical and experimental interest although still poorly understood. Most of the investigations carried out to date have been devoted to the conjugate gaze mechanism, pupillary dilatation as related to the autonomic nervous system, and the pupillary light reflex. Little attention has been given to the anatomical pathways involved in convergence, divergence, and the "near" reflex. Several authors have obtained convergence from faradic stimulation of the cerebral cortex in the cat, the monkey, the chimpanzee, and man (Schäfer, 1888a; Russel, 1894; Leyton and Sherrington, '17; Spiegel and Scala, '37; Rasmussen and Penfield, '48). A few authors have obtained divergence from cortical stimulation in the cat and monkey (Spiegel and Scala, '37; Crosby, Yoss and Henderson, '52). However, their findings were reported incidental to other studies. An extensive study of the literature revealed no systematic neuroanatomical study of these oculomotor functions. Pupillary constriction from cortical stimulation has been studied extensively in the cat, but apparently in no other animal (Wang, Lu and Lau, '31; Barris, '36). Moreover, only two studies of accommodation of the eyes produced by brain stimulation have been found in the literature (Hensen and Völckers, 1878; Bender and Weinstein, '43). The present experiments were undertaken to initiate an investigation of these phenomena in the *Macaca mulatta*.

MATERIAL AND METHODS

The experimental subjects of this research were healthy, alert macaque mon-

keys (*Macaca mulatta*). This animal was chosen because its visual system is representative of the primate series and in many ways similar to that of man. The visual fields of the eyes of the macaque overlap considerably, and binocular vision undoubtedly exists. Also, the macaque possesses the so-called near reflex and has large amplitudes of accommodation (see table 1) and convergence.

Fourteen experiments were performed on 9 monkeys (see table 2). In each experiment the monkey's head was rigidly fixed with ear plugs and a mouth bit. The drapes were arranged carefully to facilitate observation of the eyes. All experiments were carried out employing careful aseptic techniques. Isotonic saline was employed to keep the corneas moist and clear. The anesthetic used in all the experiments was ether. Every attempt was made to maintain a level of anesthesia no deeper than the point where voluntary ocular movements were abolished (Henderson, '49). In every operation a skin flap was laid back and the calvarium trephined with a dental drill. The trephine opening was enlarged the necessary amount with a rongeur. A dural flap was made exposing the underlying cortex. After completion of the experiment the dura was sutured using interrupted silk thread. The subcutaneous tissue, muscle, and skin were then sutured in

¹ Accepted in part fulfillment of the requirements for the degree of Doctor of Philosophy at the University of Michigan.

² Funds for technical help were provided by U. S. Public Health Service grant B-1442. The author wishes to express his appreciation to Parke, Davis and Company for aid in carrying on this research.

³ Author's present address is the State University of New York, Downstate Medical Center, 450 Clarkson Avenue, Brooklyn 3, New York.

layers employing a running lock stitch. A cotton strip was sutured to the closed wound edges and coated with collodion. Care was taken to prevent postoperative infection.

A Grass stimulator, model S4B, attached to a monopolar platinum electrode was employed. The indifferent electrode was placed in the rectum. This instrument generates monophasic or biphasic wave forms with variable voltage, frequency, and pulse duration. The electrode was utilized for both cortical stimulation and cortical destruction. For stimulation a frequency range from 30 to 60 vibrations per second and a strength of stimulus varying between three and 7 volts were used. Duration of the square wave pulse was one millisecond. Lesions were made by electro-coagulation and/or removal of small areas with suction. Gelfoam was employed to stop hemorrhage when necessary and to cover over dural defects.

The monkeys were observed for signs of oculomotor and pupillary abnormalities. They were sacrificed about three weeks after completion of the last experiment, unless some complication forced an earlier sacrifice.

The animals were sacrificed by first giving a hypnotic dose of sodium pentothal and then perfusing their arterial systems with 500 to 1000 cm³ of 10% formalin. The brain was then carefully removed and placed in 10% formalin for at least two weeks prior to staining. Each brain was photographed and prepared by the Marchi

technique, using the Swank and Davenport ('35) modification of this method.

Pupillary reactions and eye movements were observed and their amplitudes estimated. Accommodation was detected using a self-illuminating retinoscope (spot) at a working distance of approximately 66 cm. The reader is referred to a paper by Johnson ('35) for an explanation of the principles underlying retinoscopy. Since it was not practical to measure accommodation employing retinoscopy by interposing lenses between the eye of the observer and the eye of the monkey during an experiment the following technique was evolved: Attention was directed only to the retinoscopic reflex in the 90° corneal meridian. The refractive errors of the monkeys were measured under light ether anesthesia, and ranged from +0.50 to -2.00 diopters in the 90° corneal meridian (see table 1). A definite "with" motion of the retinoscopic reflex, equivalent to one diopter of hyperopia, was then produced either by incompletely correcting the monkey's refractive error for the observer's working distance or by holding a suitable lens in front of the monkey's eye. With this technique, neither increases in accommodation of less than one diopter nor decreases in accommodation could be detected, since such changes would not result in a change in the direction of the motion of the retinoscopic reflex. If, however, faradic stimulation of the cortex and the midbrain was sufficient to cause a change in direction of the retinoscopic reflex from a "with" to an "against"

TABLE 1
Refractive errors and accommodative amplitudes of experimental animals

Monkey	Weight	Sex	Refractive error O.D. ¹	Refractive error O.D. with 1% atropine ²	Accommodative amplitude O.S. with 1% eserine ³
	<i>pounds</i>				
107	5½	M	-2.00		
108	4	F	-0.50		
109	3½	M	+0.25		
110	4	F	-1.25		
111	5	F	+0.25		
112	4	M	-1.50	-1.50 sph. -0.50 cyl. ax. 90	5D
113	3½	M	-0.50	-0.75 sph.	7D
114	3½	M	-0.75	-1.00 sph. -0.25 cyl. ax. 90	6D
115	5	M	+0.50	+0.50 sph.	3D

¹ This was measured in the vertical meridian without cycloplegia under ether anesthesia.

² This was measured just before sacrificing the monkey under sodium pentothal anesthesia.

³ The accommodative amplitude was measured until the increasing miosis interfered with the retinoscopy. This was done just prior to sacrificing the monkey under sodium pentothal anesthesia.

motion, increased accommodation of more than one diopter was assumed to have taken place. No attempt was made to detect decreases in accommodation or to quantify the accommodative changes observed in these experiments.

For a study of this kind, it is difficult to make all measurements along the line of sight of the accommodating eye. If the eye moves at the same time that the animal accommodates (as a result of faradic stimulation of the brain), it is necessary to move the axis of the device which measures the refractive state. In this way the device remains coincident with the line of sight of the monkey's eye. Preliminary experiments with a Fincham coincidence optometer demonstrated that this instrument was not adaptable for the purposes of these experiments. Consequently, the technique with a portable (hand) retinoscope described above was adopted, and this proved quite satisfactory.

PERTINENT LITERATURE

Literature on convergence

Schäfer (1888a) obtained a slight convergence of the visual axes by stimulating at the same time corresponding points in both occipital lobes of the monkey. Mott and Schäfer (1890), working with the monkey, stimulated simultaneously and equally corresponding points in both frontal lobes and in both occipital lobes which, when stimulated individually, would produce lateral conjugate gaze. When successfully accomplished, this produced parallelism and fixation of the visual axes and no movement if the eyes were already in the primary position. If, however, the electrodes were placed on those zones which gave, on unilateral stimulation, downward or upward inclination of the visual axes combined with lateral movements, the deviation produced on bilateral stimulation was a conjugate downward or upward movement. They also obtained occasionally, on simultaneous stimulation of the frontal areas, slight convergence of the optic axes. Russel (1894), using the monkey and performing experiments suggested by Hughlings Jackson, stimulated unilaterally the frontal oculomotor regions after precluding lateral conjugate movements by

cutting the internal and the external recti in varying combinations in the two eyes. He was able to obtain direct upward and direct downward movements, as well as movements of convergence. The convergence movements were not constantly present, but were quite distinct. They were obtained from a focus overlying the most caudal part of the principal fissure and consisted of an adduction of both eyeballs with a slight inclination downward. Though Russel does not make it clear in his paper, it is assumed that these convergence movements were obtained after cutting the external rectus in each eye. Leyton and Sherrington ('17) obtained convergence of the eyeballs in the chimpanzee and the gibbon from unilateral stimulation in the frontal eye field. On one occasion, Rasmussen and Penfield ('48) obtained convergence from unilateral stimulation of the Rolandic lip of the human precentral gyrus. Thus, convergence has been produced by bilateral stimulation of the frontal and the occipital cortices, and also by unilateral stimulation in the frontal cortex.

Physical trauma and x-radiation of the occipital lobes have been reported to produce paralysis of convergence both with and without accommodation paresis (Feigenbaum and Kornbleuth, '46; Vandergrift and Losey, '22; Holmes, '18). From a clinical case, Feigenbaum and Kornbleuth ('46) concluded that a supranuclear center for convergence was present in the occipital region.

Spiegel and Scala ('36, '37) proved that ocular movements elicited from cortical stimulation were not due to spread of current to the subcortical white matter or the basal ganglia. They then demonstrated in the cat that, after total transverse section of the brain stem behind the midbrain, cortical stimulation no longer induced horizontal conjugate movements, but only vertical or convergence movements. In the experiments on the cat, they also noticed movements of divergence and unilateral upward movement of one eye from stimulation of the anterior sigmoidal gyrus. Moreover, after placing lesions in the corticofugal fibers to the nuclei of the posterior commissure, stimulation of the cortical oculomotor centers produced con-

vergence and divergence, as well as horizontal movements. Spiegel and Scala ('37) also obtained convergence from stimulating the midbrain in the cat.

Convergence has been retained in patients after extensive lesions of the pons and of the medial longitudinal fasciculus (Reese and Yaskin, '41; also present, in author's experience, in gliomas of the pons). Also, convergence and conjugate gaze may be dissociated in lesions of the medial longitudinal fasciculus, i.e., preservation of convergence with impairment of conjugate gaze in the horizontal plane in the so-called internuclear ophthalmoplegias seen commonly in multiple sclerosis. Finally, lesions in the vicinity of the superior colliculi (pinealomas) frequently produce paralysis of convergence and fixed pupils.

Thus, convergence movements are apparently not dependent upon the ascending fibers in the medial longitudinal fasciculus, as is conjugate horizontal gaze, and pontine rhombencephalic neuron arcs are dispensable for this mechanism. Rarely, stimulation in the midbrain has produced convergence in the cat, and lesions of the midbrain have produced convergence paralysis. The precise area in the midbrain is not known.

Perlia's nucleus, the unpaired motor cells lying between the lateral limbs of the third nerve nucleus, has been assumed to be the convergence "center," but recent work presents evidence to suggest that this is not true. Crosby and Woodburne ('43) found it difficult to distinguish a central nucleus in the oculomotor complex, corresponding to that of Perlia's, in either man or monkey. Warwick ('55) showed that a median nucleus of Perlia was usually absent in the monkey, though discernible in a minority of monkey midbrains, and was poorly defined in man and the chimpanzee. Also, Warwick noted that, in the few monkeys where a recognizable central nucleus did occur, its nerve cells were not internuncial and were of lower motor neuron type. These cells contributed fibers to the oculomotor nerve. He stated that these fibers innervate the superior rectus and the inferior oblique muscles and not the medial recti in the monkey. He concluded that the central

nucleus, when it did occur, was not an integrative center for convergence in the monkey.

Literature on divergence

Parsons ('01), in his paper on dilatation of the pupil from stimulation of the frontal cortex of the monkey, noted, on occasion, unilateral movement of one eye up and out associated with pupillary dilatation. Spiegel and Scala ('36, '37) reported divergence movements in the cat from stimulating the anterior sigmoidal gyrus. Bender (quoted in Bender and Savitsky, '40) observed divergence and miosis in the monkey from stimulation of one side of the cortex at the parieto-occipital junction. Crosby, Yoss and Henderson ('52) obtained divergence movements from unilateral stimulation in the frontal eye fields. Bender and Savitsky ('40) reported a patient with a divergence paralysis who, at autopsy, had a small cavernous hemangioma in the tegmentum of the midbrain.

Literature on accommodation

A dioptric change in the direction of myopia has been produced by stimulation of the intracranial portion of the oculomotor nerve. This was measured by retinoscopy (Morgan, Olmsted and Watrous, '40; Kuntz, Richins and Casey, '46). It has also been produced by stimulation of the ciliary ganglion (Marg, '54; Marg, Reeves and Wendt, '55), the short posterior ciliary nerves (Olmsted, '44), and around the entrance of the optic nerve into the globe (Allen, '50).

Stimulation of the cervical sympathetic trunk has resulted in a flattening of the lens and hyperopia (Olmsted, '44; Cogan, '37). In human subjects mild faradic stimulation of the skin of the forearm or the fingertips elicits a dioptric change of small magnitude in the direction of hyperopia. Kuntz, Richins and Casey ('46) presented evidence that the oculomotor nerve in the cat possesses both cholinergic and adrenergic fibers and that the hyperopia is the result of reflex inhibition of the ciliary muscle mediated through the parasympathetic innervation of the eye. This implied that there was some conduction of efferent impulses from the ciliary ganglion to the ciliary muscle

through the adrenergic component of the short ciliary nerves.

Hensen and Völkers (1878) obtained accommodation of the eyes in a dog by stimulating the posterior part of the wall of the third ventricle. In the monkey Bender and Weinstein ('43) obtained conspicuous bulging of both irises, unaccompanied by pupillary constriction or convergence, with stimulation of a point at the midventral and midsagittal planes of the oculomotor nucleus (Edinger-Westphal nucleus) 1 mm below the focus for pupillary constriction. The bulge was greatest at the pupillary margin and receded sharply when the current was stopped. They presumed that the bulge in the iris was due to contraction of the ciliary muscle, and that the motor neurons supplying the ciliary muscle probably have a distinct localization in the Edinger-Westphal nucleus below the center for pupillary constriction.

Literature on pupillary constriction

Pupillary constriction resulting from stimulation of the frontal lobe has rarely been reported. Spiegel and Takano ('29) usually obtained dilatation of the pupil in the cat from stimulating the corticofugal fibers emanating from the frontal cortex. However, on one occasion, they demonstrated pupillary constriction associated with conjugate deviation of the eyes to the opposite side. If the corticofugal fibers were then permitted to degenerate, pupillomotor activity could not be elicited from stimulating the caudate nucleus. Therefore, they concluded that the fibers for pupillary movement made their way to the midbrain or pons without synapse in the caudate nucleus. Hodes and Magoun ('42b) obtained pupilloconstrictor responses in the cat from the anterior portion of the gyrus cinguli and from the adjacent part of the gyrus genualis. These areas overlapped to some extent the field for pupillodilatation.

On a number of occasions stimulation of the occipital lobe has been reported to produce pupillary constriction. Schäfer (1888b) occasionally obtained marked contraction of the pupils in the monkey from stimulation on or near the quadrate lobe. Wang, Lu and Lau ('31) stimulated

a restricted area on the gyrus compositus posterior of the cat and induced constriction of both pupils. In the cat, Barris ('36) obtained bilateral and equal pupillary constriction from stimulation of the lower end of the inferior portion of the posterior lateral gyrus. The degree of pupillary constriction was never greater than from $\frac{1}{2}$ to $\frac{1}{3}$ the original diameters of the pupils and could be re-elicited upon repeated stimulation. However, the cortex eventually became injured or fatigued, and then further stimulation produced no pupillomotor activity. Simultaneous stimulation of the responsive cortex on both sides resulted in an augmentation of the amplitude of constriction of both pupils to about one half of their original size. Barris then excised the cortical areas responsible for pupillary constriction and, using the Marchi technique, traced fibers originating in those areas along the lateral wall of the lateral ventricle, over the lateral geniculate body, and through the stratum zonale of the thalamus to the pretectal area. He found the cortical fibers aggregated into a small fascicle in the wall of the lateral ventricle. Hare, Magoun and Ranson ('35) had previously obtained pupillary constriction from stimulating the white matter in the lateral wall of the lateral ventricle. They believed that this constriction was due to stimulation of efferent fibers of cortical origin. Barris ('36) suggested that Hare, Magoun and Ranson ('35) were stimulating the fascicle of fibers that he had detected in the wall of the lateral ventricle. Waller and Barris ('37) produced anisocoria by ablation of the pupilloconstrictor zone in the cat. The larger pupil was on the side opposite the lesion and was more responsive to light and painful stimuli. Bender (quoted from Bender and Savitsky, '40) obtained miosis with some divergence by stimulation of the cortex at the parieto-occipital junction in the monkey.

Pupillary constriction has been obtained by stimulating the pretectal region and the oculomotor nuclear complex in the midbrain. Ranson and Magoun ('33b), in the cat, and Magoun, Atlas, Hare and Ranson ('36), in the monkey, obtained constrictor responses from faradic stimulation of the optic chiasm, of the optic tract

on the lateral surface of the brain stem and ventral to the lateral geniculate body, of the brachium of the superior colliculus, of the pretectal region, and of the posterior commissure and the fibers emerging from it and arching around the central gray matter at the level of transition between the third ventricle and the cerebral aqueduct. They also demonstrated pupillary constriction from stimulation of the oculomotor nerve. Marked bilateral constriction was elicited by stimulation of the posterior commissure and of the region dorsolateral to it but marked ipsilateral and weak contralateral constriction appeared on stimulating fibers arching ventrally around the central gray matter. These facts were interpreted as indicating that there were two decussations: an extensive one in the posterior commissure and a second, smaller and more ventrally placed crossing beneath the cerebral aqueduct. Barris, Ingram and Ranson ('35) studied serial sections of a cat's brain prepared by the Marchi staining method from which the eye had been enucleated some suitable time previously. They traced crossed and uncrossed fibers of retinal origin through the stratum zonale of the thalamus to the pretectal area, where they appeared to terminate.

Stimulation of the superior colliculi has not produced pupillary constriction (Ranson and Magoun, '33b; Magoun, Atlas, Hare and Ranson, '36). Also, destruction of the superior colliculi does not affect the pupillomotor pathway for light (Magoun and Ranson, '35; and many others). Therefore, it is apparent that the pathway for pupillary constriction does not involve the superior colliculi.

Bender and Weinstein ('43) produced pupillary constriction in the monkey by stimulation of the most rostral and dorsal portion of the oculomotor nucleus. They believed that they were stimulating the small cells of the Edinger-Westphal nucleus. They were also able to produce unilateral pupillary constriction in the same area with smaller faradic currents.

After cutting the optic nerve in the cat or rat, degenerating fibers can be traced only as far as the pretectal areas and not into the oculomotor nuclear complex (Barris, '35; Lashley, '34). Also, after sec-

tion of the optic nerve or tract in the cat, with sufficient time allowed for degeneration, successive stimulation along the pathway from the retina toward the pretectal nuclei results in pupillary constriction only after the pretectal zone is reached (Hare, Magoun and Ranson, '35). These experiments appear to demonstrate the presence of a synapse in the pretectal region and to show that impulses from both eyes reach the pretectal area.

In summary, the work done to date indicates that the pathway from the frontal cortex for pupilloconstriction does not synapse in the caudate nucleus. The fibers from the occipital cortex (cortico-pretectal pathway) travel along with other corticotectal and corticotegmental fibers by way of a small fascicle in the lateral wall of the lateral ventricle. This bundle courses over the lateral geniculate body and through the stratum zonale of the thalamus to the pretectal area where the fibers synapse.

The light reflex fibers from the retina traverse the portion of the optic tract which runs medial to the lateral geniculate body, and pass caudally along the lateral and dorsal aspects of the medial geniculate body to reach the brachium of the superior colliculus. After reaching the brachium the light reflex fibers do not enter the superior colliculus itself, but turn rostrally and medially into the pretectal region or the transition areas between the thalamus and midbrain where they synapse. Thus, the pretectal nuclei situated under cover of the anterior and lateral margin of the superior colliculi at the tecto-thalamic junction appear to be centers for the transmission of afferent pupillary impulses from the retinas to the Edinger-Westphal nuclei.

From the pretectal region the fibers descend around the rostral end of the central gray matter of the aqueduct to terminate in the Edinger-Westphal nuclei. Central crossings in the pathway were found to occur both in the posterior commissure and ventral to the cerebral aqueduct in the immediate vicinity of the oculomotor nuclei (Magoun, Atlas, Hare and Ranson, '36).

Topographically, the rostral Edinger-Westphal nucleus passes into the caudal

Edinger-Westphal nucleus without clear separation. These nuclei consist of medium-sized, stellate to spindle-shaped multipolar neurons with Nissl granules resembling those seen in other preganglionic neurons (Crosby and Woodburne, '43). From the paired Edinger-Westphal nuclei emanate nerve fibers which enter the oculomotor nerves (Crouch, '36; Warwick, '54). Crouch ('36) found both crossed and uncrossed fibers but Warwick ('54) could detect only uncrossed fibers issuing from the Edinger-Westphal and anterior median nucleus (rostral Edinger-Westphal nucleus). These fibers probably take up a superficial position around the oculomotor nerve in the anterior cavernous sinus, superior orbital fissure, and orbit (Sunderland and Hughes, '46). They then travel in the inferior division of the oculomotor nerve and the nerve to the inferior oblique muscle and reach the ciliary ganglion via its motor root (Warwick, '54). From the ciliary ganglion postganglionic fibers have been traced to the intrinsic eye muscles—the ciliary muscle and the sphincter of the iris (Clark, '37; Stotler, '37). Warwick found that practically all the cells in the ciliary ganglion innervate intrinsic ocular musculature, but that only a small fraction of their axons supply the sphincter of the pupil. Situated in proximity to the posterior ciliary nerves—either sclerally, episclerally, or a short distance removed from the globe—is the accessory ganglion of Axenfeld (Givner, '39). Also, there are ganglion cells within the globe at the root of the iris and ciliary body (Wolter, personal communication).

A unilateral dissociated pupil, i.e., a pupil that fails to constrict on exposure to light but constricts with accommodation and convergence, may result from orbital injury (Nathan and Turner, '42). Removal of the ciliary ganglion in apes results in a similar type of dissociated pupil (Foerster, Gagel and Mahoney, '36). These facts have been interpreted to mean that there are two peripheral efferent pathways for pupillary constriction; one serving the light reflex, the other serving the accommodation-convergence synkinesis. The accessory ganglion of Axenfeld or the intraocular ganglion cells, or both, have

been incriminated as intermediate stations in the second pathway.

Literature on pupillary dilatation

Pupillary dilatation has been produced by stimulation of the prefrontal, sensory, auditory, and occipital cortices, but most studies to date have been devoted to the frontal cortex. In the cat, the dog, and the monkey, with minimal anesthesia, Parsons ('01) obtained dilatation of the pupils from stimulation of the frontal oculomotor area and of the occipital visual center. He was able to obtain pupillary dilatation from other cortical areas only when they were associated with violent, generalized convulsive movements. He noted bilateral pupillary dilatation associated with or without conjugate ocular movement and found that the degree of pupillary dilatation was often greater in the eye contralateral to stimulation. Wang, Lu and Lau ('32) produced pupilodilatation in the cat only from stimulating the sigmoid convolution. This was also noted by Claes ('39b). Hodes and Magoun ('42a; '42b) outlined a dilator field located in the gyri proreus and genualis of the frontal cortex of the cat with a caudal continuation extending backward through the basal telencephalon to the hypothalamus. Ward and Reed ('46) produced bilateral pupillary dilatation in the monkey from the tip of the arcuate sulcus where it extended over onto the medial surface of the superior frontal convolution and throughout the extent of Brodmann's area 32. Keller ('44) noted in the cat that bilateral de-cortication produced miosis. Ten Cate ('34) noted pupillary dilatation on stimulating the auditory cortex of the cat.

The exact mechanism for pupillary dilatation resulting from stimulation of the frontal eye field is not yet entirely agreed upon by all interested observers. This is also true for pupillary dilatation produced by pain, emotion, or by stimulation of peripheral nerves. Section of the cervical sympathetic in the monkey abolishes pupillary dilatation otherwise produced by stimulating the frontal cortex or aroused by painful stimuli or emotion (Weinstein and Bender, '41; Ward and Reed, '46). However, Ward and Reed ('46) produced slight dilatation of the pupils by stimu-

lating the frontal cortex in the monkey after sympathectomy under special conditions of anesthesia. They maintained that the pathway governing the inhibitory dilatation was a direct projection system to the oculomotor nucleus. Kuntz, Richins and Casey ('46) demonstrated both cholinergic and adrenergic fibers in the oculomotor nerve. In the cat, bilateral sympathectomy did not impair pupillary dilatation due to stimulation of the frontal cortex arising as the result of painful and emotional stimuli (Hodes, '40; Hodes and Magoun, '42b). Weinstein and Bender ('41) concluded that in the cat and the monkey pupillary dilatation is accomplished by both parasympathetic inhibitory and sympathetic excitatory mechanisms. In the cat, inhibition of the parasympathetic mechanism was of greater importance. There was, thus, a species variation. The anesthetic used may excite or depress the ciliospinal center and determine the level of sympathetic pupillary activity (Kuntz and Richins, '46).

Claes ('39a) obtained bilateral pupillary dilatation in the cat, unassociated with eye movement, by stimulation of the inferomedial part of the internal capsule. The dilatation was more marked than that obtained from stimulating the inferior colliculi. Pupillary dilatation was readily obtained by hypothalamic stimulation and this dilatation was not eliminated by decerebration (Karplus and Kriedl, '10; Spiegel and Hunsicker, '36). Ranson and Magoun ('33a) obtained marked bilateral dilatation of the pupils from the lateral hypothalamic area and the region surrounding the fornix. Pupillary dilatation was elicited at the level of the anterior hypothalamic nucleus and from the lateral hypothalamic area caudal to this level. Dilatation was also elicited at the transition from the hypothalamus to the midbrain and at scattered points throughout the tegmentum of the midbrain and the pons. Pupillary dilatation was likewise obtained from stimulating the basal telencephalon, the midline part of the thalamus, and the subthalamus (Hodes and Magoun, '42b). Unilateral hypothalamic stimulation produced pupillary dilatation predominantly on the same side (Beattie, Duell and Ballance, '32). Ingram, Ranson and

Hannett ('31) obtained pupillary dilatation by stimulation of the midbrain tegmentum, the reticular substance of the pons and the medulla, and the upper cervical cord. Beattie, Brow and Long ('30) and Foerster ('28) noted homolateral pupillary dilatation on stimulation of the anterolateral column of the cervical spinal cord. Sectioning the cervical cord abolished pupillary dilatation produced by hypothalamic stimulation (Beattie, Brow and Long, '30). Thus, the hypothalamic center produced its effect by sympathetic excitation and not by parasympathetic stimulation.

In the cat, Claes ('39b) produced bilateral and equal pupillary dilatation by stimulation of the inferior colliculi. Since section of the cervical sympathetic did not eliminate this response, Claes assumed it was the result of inhibition of the Edinger-Westphal nucleus. Harris, Hodes and Magoun ('44) demonstrated the presence of inhibitory fibers in the spinal cord. These fibers traversed the reticular substance of the brain stem and spinal cord to reach the midbrain.

Thus, it is probable that there are at least two separate nervous pathways from the frontal cortex governing pupillary dilatation. One acts as an inhibitor of parasympathetic centers, going directly to the midbrain (Ward and Reed, '46) and utilizing the adrenergic component of the oculomotor nerve (Kuntz, Richins and Casey, '46), and the other influences the sympathetic centers of the cervical cord and is excitatory. This latter probably is a multisynaptic system which synapses in course in the midbrain and possibly in other brain centers (Harris, Hodes and Magoun, '44). Another system having presumably an inhibitory effect is that from the inferior colliculi mediating pupillary dilatation from acoustic stimuli (Claes, '39b).

In summary, the sympathetic fibers for pupillary dilatation from the frontal cortex remain uncrossed and pass through the inferomedial part of the internal capsule making a number of synapses in the diencephalon. The hypothalamic connections appear diffuse although more concentrated rostrally than caudally. From the hypothalamus the fibers run dorsally

in the tegmentum of the midbrain, the reticular substance of the pons and medulla, and possibly in the dorsal longitudinal fasciculus (Ingram, Ranson and Hannett, '31) to the cervical cord. In the cervical cord, fibers course in the ventrolateral column to the ciliospinal center at cervical segments 7 and 8 and thoracic segment 1. From the ciliospinal center the preganglionic fibers ascend in the cervical sympathetic trunk to make synapse in the superior cervical ganglion. The postganglionic fibers travel via the internal carotid plexus surrounding the internal carotid artery to cross through the middle ear and then proceed to the cavernous sinus where the cavernous plexus is formed (Kuntz, '53). Thence fibers are distributed along the ophthalmic division of the trigeminal nerve and reach the iris via the ciliary ganglion.

EXPERIMENTAL RESULTS

The configurations of the frontal and the occipital eye fields are indicated diagrammatically in figures 1 through 5. These figures should be referred to in connection with the following account of the experiments. Tables 1 and 2 will provide some ancillary data concerning the experiments and the experimental subjects. The brain map utilized is that of Brodmann for Cercopithecus and is contained in the monograph of Bonin and Bailey ('47).

Cortical lesions were placed in the frontal, the temporal, and the occipital eye fields. The positions of the lesions are indicated in figures 1 and 2 and in figures 8 through 11. Study of the Marchi preparations confirmed the previous work by Crosby and Henderson ('48); Crosby, Yoss and Henderson ('52); and Crosby ('56) on the projections of these cortical fields. These findings will be briefly discussed in the final paragraphs below. Post-operative ocular abnormalities were observed following 5 operations. These are listed in table 3.

Experiment no. 1 (table 2, monkey 107). Stimulation of the frontal cortex at point A in figure 1, in the area that usually gives conjugate contralateral oblique upward movements (Crosby, Yoss and Henderson, '52), produced bilateral equal dilatation of the pupils (from about 4 mm to 6 mm). This area is in the second motor frontal eye area (Crosby, '56). When the stimulation was extended into the region of the arcuate fissure (fig. 1, point B) there was bilateral equal dilatation of the pupils accompanied by bilateral and equal partial tonic closure of both eyelids. The experiment was curtailed when the animal regained sufficient consciousness to break out of the ear plugs.

Experiment no. 2 (table 2, monkey 108). Faradic stimulation was carried out above and below the principal fissure. Stimulation of point C in figure 1 resulted in dila-

TABLE 2
Ancillary data on experiments

Exp. no.	Monkey	Weight pounds	Sex	Date of experiment	Site of operation	Previous operation	Date sacrificed
1	107	5½	M	10/ 7/57	right frontal	none	10/28/57
2	108	4	F	10/14/57	left frontal	none	11/18/57
3	108	4	F	10/28/57	right occipital	10/14/57	11/18/57
4	109	3½	M	11/ 4/57	right occipital	none	11/26/57
5	110	4	F	11/11/57	left occipital	none	12/17/57
6	110	4	F	11/25/57	right frontal	11/11/57	12/17/57
7	111	5	F	12/ 2/57	left occipital	none	1/10/58
8	111	5	F	12/16/57	right frontal	12/ 2/57	1/10/58
9	112	4	M	1/13/58	right occipital	none	1/19/58
10	113	3½	M	1/29/58	right occipital	none	3/11/58
11	113	3½	M	2/17/58	left occipital	1/29/58	3/11/58
12	114	3½	M	2/ 3/58	midbrain (right occipital hemispherectomy)	none	3/18/58
13	114	3½	M	2/24/58	left frontal	2/ 3/58	3/18/58
14	115	5	M	3/10/58	left frontal and right occipital	none	3/25/58

tation of the contralateral pupil (from approximately 5 mm to 7 mm) and contralateral partial tonic lid closure. These movements were accompanied by slight closure of the left lid without any perceptible change in the size of the homolateral pupil. Sneering movements of the contralateral side of the face were obtained when the stimulus was shifted across the arcuate fissure into the precentral gyrus. Slightly shifting the stimulating electrode in a cephalic direction resulted in conjugate deviation of the eyes to the contralateral side with simultaneous dilatation of the pupils that was greater in the contralateral eye than in the homolateral eye. No accommodation was noted with the retinoscope. Stimulation of point D in figure 1 produced bilateral and equal dilatation of the pupils (from approximately 5 mm to 7 mm) accompanied by bilateral partial tonic lid closure. When the stimulus was carried caudally to point E in figure 1, bilateral and equal sneering movements of the face were produced. The eyes remained in the straight ahead or primary position. No accommodation was noted with the retinoscope.

Experiment no. 3 (table 2, monkey 108). Faradic stimulation was carried out in the temporal-occipital transition area and in the occipital lobe in areas 18, 19 and 22 of Brodmann. Stimulation of point F in figure 1 in area 18 of Brodmann resulted in bilateral and equal dilatation of the pupils (from about 5 mm to 7 mm), with the eyes remaining fixed in the straight ahead position. Stimulation of points G and H in figure 1 (adjoining this area 18 rostrally) in area 19 of Brodmann and caudally in the region of the lunate sulcus produced horizontal conjugate deviation of the eyes to the contralateral side. With this conjugate deviation no pupillary or accommodative changes were noted. Stimulation of points K and L in figure 1 produced conjugate deviation of the eyes to the contralateral side and down. No pupillary changes were noted. Since there was no detectable change noted in the retinoscopic reflex for any of the points stimulated accommodation was assumed not to have taken place.

Stimulation in area 19 of Brodmann, farther rostrally in the region of point X

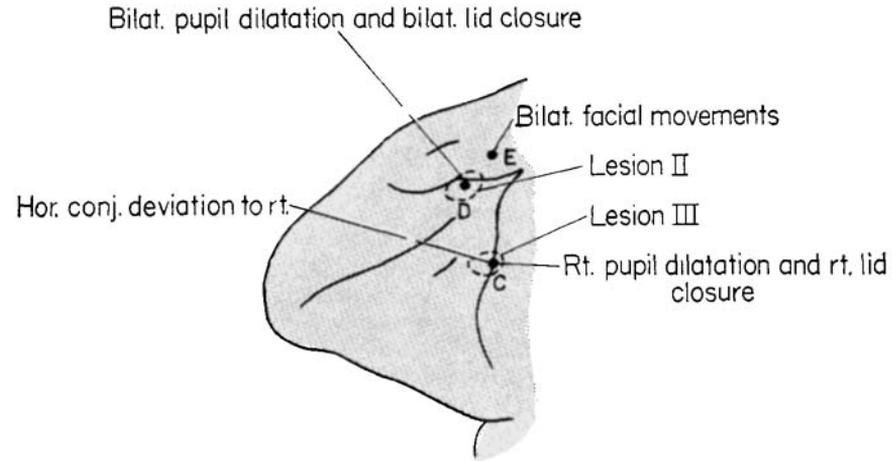
in figure 1, resulted in convergence movements accompanied by bilateral equal pupillary constriction of about $\frac{1}{3}$ the original pupillary diameter. The amplitude of adduction was from 10 to 15 degrees in the homolateral eye and about 5 degrees in the contralateral eye. Varying the strength of the stimulus and shifting it slightly produced adduction in the homolateral eye without any movement in the contralateral eye (homolateral adduction) and associated bilateral and equal pupillary constriction. No symmetrical convergence was noted. In this region bilateral pupillary constriction was also obtained as an isolated phenomenon without convergence movements. Increasing the strength and slightly shifting the stimulus in this area occasionally resulted in a horizontal deviation of the eyes to the contralateral side; in this deviation the amplitude and the velocity of the movements were greater in the homolateral eye. In this region abrupt change in the retinoscopic reflex (from a "with" to an "against" motion) was noted indicating that accommodation had taken place. The return of the accommodation to a state comparable to that prior to stimulation was slow compared to the convergence movements and pupillary constriction.

Stimulation in area 22 of Brodmann at point Y in figure 1 adjoining the above area in the superior temporal gyrus produced responses similar to those described above: convergence, pupillary constriction and accommodation.

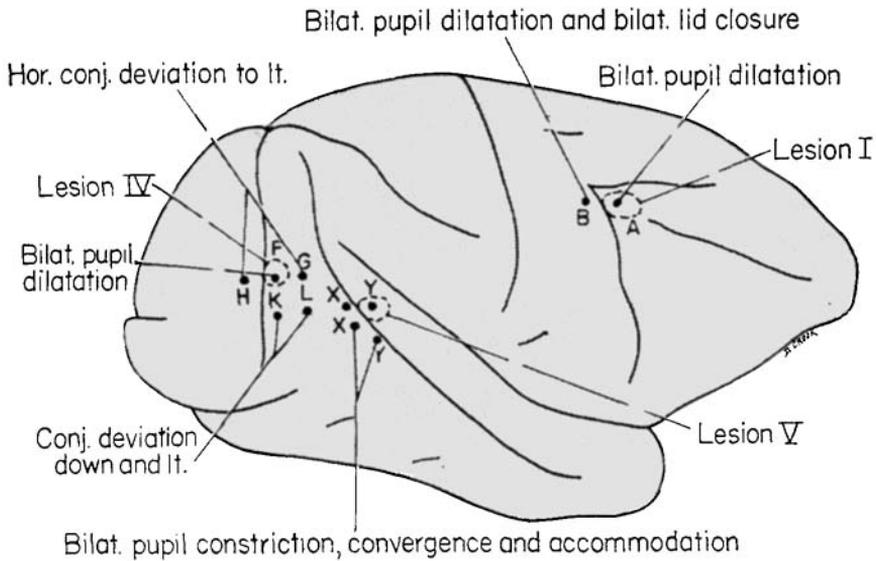
Experiment no. 4 (table 2, monkey 109). Faradic stimulation was carried out in the parieto-occipital transition area and in the occipital lobe in areas 17 and 19 of Brodmann. Stimulation of point X in figure 2 (this area was near the most superior part of the superior temporal fissure) resulted in pupillary constriction (approximately 6 mm to 4 mm) that was equal in the two eyes. When stimulation ceased, the pupils promptly regained their original diameters. By varying the strength of the stimulus, and by slight variation in the precise point of stimulation, three types of convergence movements were elicited from this area. The most frequent was bilateral adduction with the greater amplitude in the homolateral eye. The next was homolateral ad-

duction with no observable movement in the contralateral eye. Only on one occasion was bilateral equal adduction of small amplitude noted. The convergence movements were usually associated with pu-

pillary constriction but were also noted without any pupillary changes. After a convergence movement, with cessation of the stimulus, the eyes returned rather slowly to the straight ahead position. In-



LT. FRONTAL LOBE



RT. HEMISPHERE

Fig. 1 A drawing of the right and left cerebral hemispheres of *Macaca mulatta* illustrating the findings in experiments 1, 2, and 3 in monkey no. 107 and monkey no. 108. Lesion I was made in monkey no. 107. Lesions II and III were made in monkey no. 108. Bilat., bilateral; conj., conjugate; hor., horizontal; Lt., left; Rt., right.

creasing the strength of the stimulus above a certain level resulted in horizontal conjugate deviations of the eyes to the contralateral side. In this conjugate deviation the amplitude of movement on a few occasions was greater in the homolateral eye.

Accommodation was observed in the same region. This was manifested by an abrupt reversal of the retinoscopic reflex (from a "with" to an "against" movement). The disappearance of retinoscopic evidence of accommodation was not so prompt as the return of the pupils (the most prompt) and of the eyes themselves to their state prior to stimulation. It was necessary to wait a few minutes for evidence of the disappearance of accommodation (retinoscopic evidence of a return to a "with" motion).

Experiment no. 5 (table 2, monkey 110). Faradic stimulation was carried out in the temporal and the occipital cortices. Stimulation of points Y in figure 2 resulted in convergence movements. The first few stimuli produced just perceptible bilateral and equal adduction of both eyes. Further stimulation resulted in a greater amplitude of adduction in the homolateral than in the contralateral eye. These asymmetrical convergence movements ranged between 5° and 10° in the homolateral eye and were just perceptible in the contralateral eye. Pupillary constriction was minimal if present at all. After cessation of the stimulus, the return of the eyes to the straight ahead position was slow. However, on one occasion, when the stimulus was stopped, there was a sudden symmetrical divergence of both eyes accompanied by a slight bilateral pupillary dilatation. The convergence movements were accompanied by accommodation (indicated by a reversal of the retinoscopic reflex from a "with" to an "against" movement). After cessation of the stimulation it was necessary to wait a few minutes for the retinoscopic signs of accommodation to disappear (that is, for the reflex to return to a "with" motion).

When point Z in figure 2, in area 18 of Brodmann (which adjoins the area just described) was stimulated, similar convergence movements and accommodation were elicited. Stimulation at point A (in fig. 2) just caudal to the lunate fissure in area 18 of Brodmann resulted in conjugate

deviation of the eyes up and to the right, associated with slight bilateral pupillary dilatation.

Experiment no. 6 (table 2, monkey 110). Stimulation was carried out toward the cephalic end of the right principal fissure in the inferior frontal gyrus in areas 8, 9, and 10 of Brodmann. Stimulation of points B in figure 2 resulted in convergence movements and pupillary constriction. The convergence movements were asymmetrical with the greater adduction observed in the contralateral eye. The pupils constricted equally to about $\frac{1}{3}$ their original diameters. After cessation of the stimulation the eyes returned slowly to a straight ahead or to a slightly divergent position and the pupils dilated. The convergence movements were always associated with pupillary constriction, but pupillary constriction was also observed as an independent phenomenon. In the same area, by increasing the strength of stimulus and a slight shifting of the electrode, it was possible to produce conjugate deviation of the eyes towards the contralateral side. It was noted that the amplitude and the velocity of this conjugate movement frequently appeared to be greater in the homolateral eye.

Stimulation slightly caudally to that just described, at point C in figure 2, resulted in divergence movements. Both eyes abducted from the primary position. The abduction in the contralateral eye was just perceptible. The abduction in the homolateral eye was estimated to be about 5 degrees. No pupillary changes accompanied these divergence movements.

Stimulation just rostral to the inferior ramus of the right arcuate sulcus in area 8 of Brodmann (point E in fig. 2) resulted in conjugate deviation of the eyes to the contralateral side. Stimulation more ventrally, at point F in figure 2, produced conjugate deviation of the eyes toward the contralateral side and downward. These conjugate deviations were associated with slight but definite bilateral and equal pupillary dilatation. In the above procedures no accommodation was noted as indicated by a reversal in the retinoscopic image.

Experiment no. 7 (table 2, monkey 111). Areas 18 and 19 of Brodmann were subjected to faradic stimulation. Stimulation

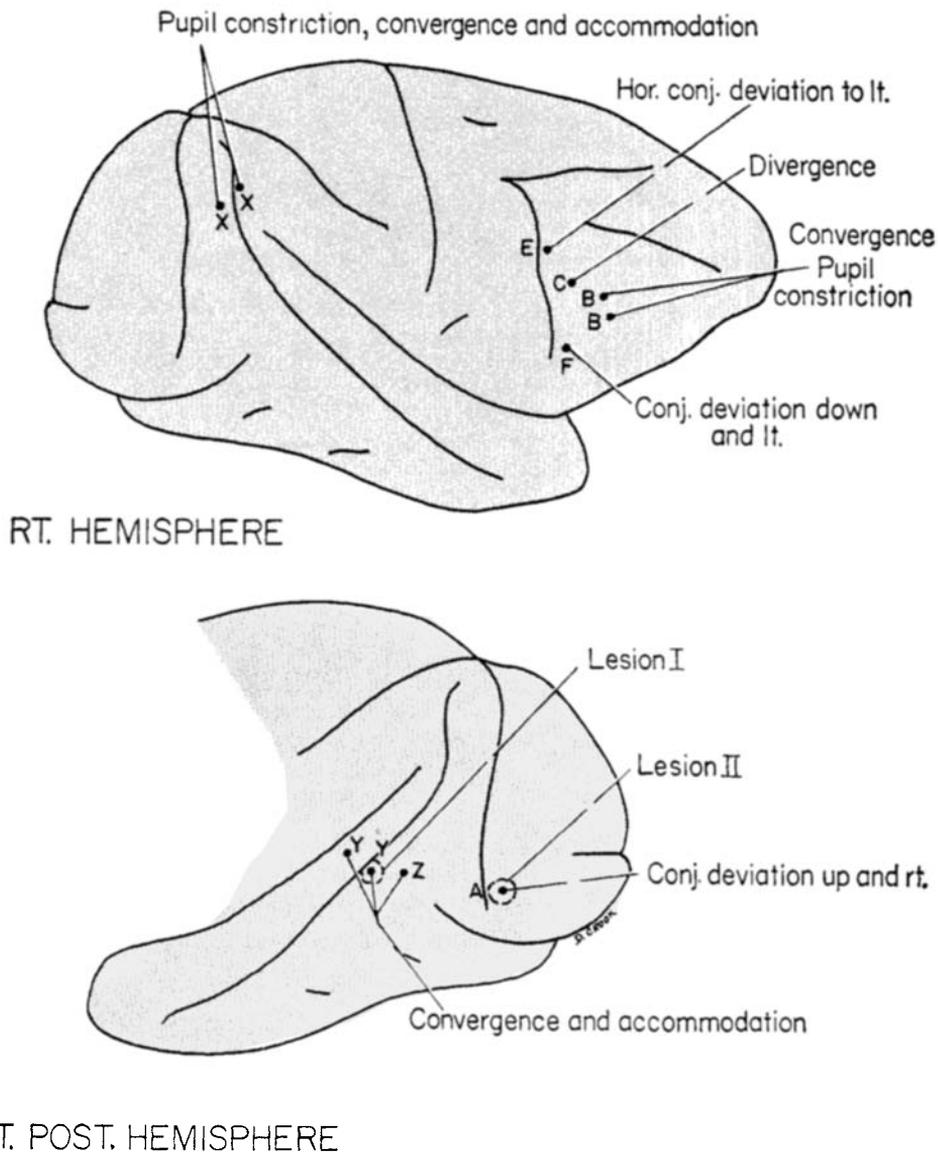


Fig. 2 A drawing of the right and left cerebral hemispheres of *Macaca mulatta* illustrating the findings in experiments 4, 5 and 6 in monkey no. 109 and monkey no. 110. Lesions I and II were made in monkey no. 110. Conj., conjugate; hor., horizontal; Lt., left; Rt., right.

of point A in figure 3, in the most superior part of area 19 just in front of the lunate fissure, resulted in conjugate deviation of the eyes upward and toward the contralateral side. Stimulation at points B in figure 3, slightly inferior to the above region and behind the lunate fissure, pro-

duced conjugate deviation of the eyes to the opposite side and downward. In the midregion, at about the level of the external calcarine sulcus, stimulation on either side of the lunate fissure gave conjugate horizontal deviation of the eyes toward the side opposite stimulation (fig. 3, point C). Stim-

ulation at point D in figure 3, below the level of the external calcarine sulcus, produced conjugate horizontal deviation of the eyes to the opposite side and upward. In each case the conjugate ocular deviations were associated with a bilateral dilatation of the pupils that was greater in the homolateral eye. These findings agree with

those of Crosby and Henderson ('48) in so far as the extraocular movements are concerned.

Stimulation of point E in figure 3, in the temporal-occipital transition area between the lunate fissure and the superior temporal sulcus, produced bilateral and equal dilatation of the pupils without eye move-

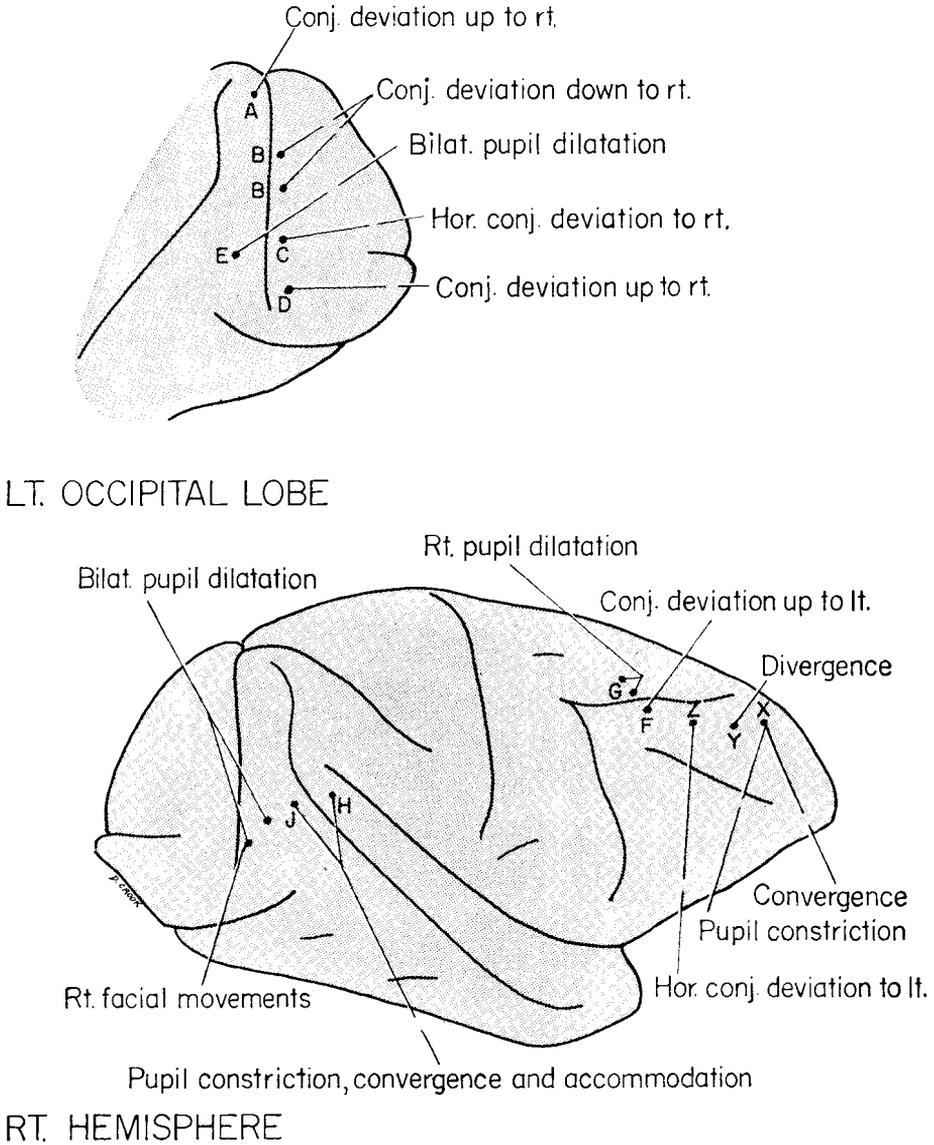


Fig. 3 A drawing of the right and left cerebral hemispheres of *Macaca mulatta* illustrating the findings in experiments 7, 8, and 9 in monkey no. 111 and monkey no. 112. Bilat., bilateral; conj., conjugate; hor., horizontal; Lt., left; Rt., right.

ments. In this series of stimulations no pupillary constriction or accommodation was noted.

Experiment no. 8 (table 2, monkey 111). The frontal cortex was stimulated in areas 8 and 9 of Brodmann. Stimulation most rostrally in the region of point X in figure 3 produced three types of convergence movements. Most often there was a bilateral adduction of greater amplitude in the homolateral eye. Occasionally there was adduction of the homolateral eye without movement in the other eye. On one occasion there was a symmetrical adduction of very small amplitude in both eyes. From the same cortical areas, there was bilateral and equal pupillary constriction from about 6 mm to 4 mm with and without accompanying divergence. No accommodation was observed with the retinoscope.

Caudal to the above area, at point Y in figure 3, stimulation resulted in abduction of the contralateral eye producing a divergence of the visual axes. More caudal to this, at point Z (right) in figure 3, stimulation produced conjugate horizontal deviation of the eyes to the left, with the velocity of the movements in the contralateral eye greater than the velocity in the homolateral eye. Associated with this conjugate deviation was bilateral and equal dilatation of the pupils. At point F, located still more caudally, there was conjugate deviation of the eyes toward the opposite side and slightly upward, associated with bilateral and equal dilatation of the pupils. Still farther caudally, extending into the region of the superior ramus of the arcuate fissure at point G in figure 3, stimulation resulted in dilatation of the homolateral pupil associated with abduction of the homolateral eye, partial closure of the homolateral lid, and sneering movements of the homolateral side of the face. No accommodation was noted.

Experiment no. 9 (table 2, monkey 112). Stimulation of point H in figure 3, in the superior temporal gyrus, resulted in convergence movements and bilateral and equal pupillary constriction. The convergence movements were of two types: bilateral adduction with the greater amplitude in the homolateral eye; adduction in the homolateral eye without noticeable movements

in the contralateral eye. The pupils constricted from about 5 mm to 3 mm. Such constriction occurred both with and without convergence movements. In the same area accommodation was manifested by an abrupt change in the retinoscopic reflex (from a "with" to an "against" movement). With cessation of the stimulation the retinoscopic examination indicated that the accommodation persisted for two to three minutes. Stimulation caudal to the superior temporal sulcus at point J in figure 3 resulted in convergence movements, pupillary constriction, and accommodation similar to that described above.

Stimulation still more caudally, about midway between the superior temporal sulcus and the lunate fissure, resulted in bilateral and equal pupillary dilatation (from about 5 mm to 7 mm) associated with movements of the lower part of the face on the homolateral side.

Experiment no. 10 (table 2, monkey 113). The cerebral cortex was noted to be hyperemic and edematous. Stimulation at points X in figure 4 in the posterior parietal and occipital lobes resulted in bilateral and equal pupillary dilatation. No convergence movements or pupillary constriction could be elicited. When strong faradic stimulation was employed, contralateral conjugate deviations of the eyes (without oblique components) occurred, associated with pupillary dilatation.

Experiment no. 11 (table 2, monkey 113). Stimulation of point Y in figure 4 resulted in convergence movements and pupillary constriction. The usual response was about 10 degrees of adduction in the homolateral eye and from three to 5 degrees in the contralateral eye. There was also adduction in the homolateral eye without movement of the contralateral eye. Bilateral and equal pupillary constriction (from about 6 mm to 4 mm) was noted as an isolated response and also associated with the convergence movements. On one occasion, from stimulation in the same area, a divergence movement consisting of abduction in the contralateral eye without movement in the homolateral eye was observed. Increasing the strength of the stimulus and shifting it slightly resulted in conjugate deviation of the eyes toward the opposite side with the greater amplitude of

movement in the homolateral eye. Accommodation was elicited from this region, as indicated by a prompt reversal of the retinoscopic reflex (from a "with" to an "against" movement). Disappearance of retinoscopic evidence of accommodation (return of the reflex to a "with" movement) after cessation of the stimulation was gradual and extended over more than one minute. This was in contrast to the

convergence movements and pupillary constriction which promptly disappeared. Stimulation at point Z caudal to the above region and behind the superior temporal gyrus resulted in convergence movements, pupillary constriction, and accommodation similar to that described above.

Experiment no. 12 (table 2, monkey 114). With suction and cautery the right occipital and the posterior parietal lobes

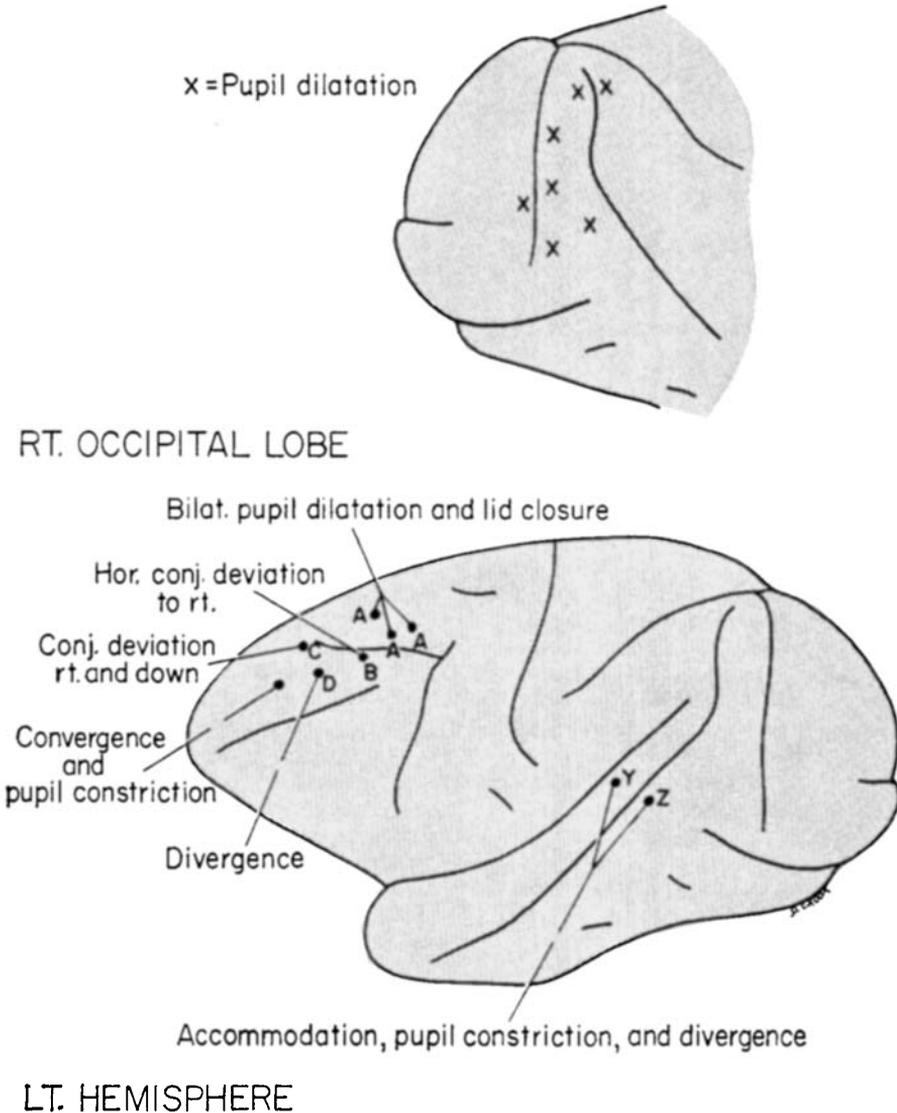


Fig. 4 A drawing of the right and left cerebral hemispheres of *Macaca mulatta* illustrating the findings in experiments 10, 11, and 13 in monkey no. 113 and monkey no. 114. Bilat., bilateral; conj., conjugate; hor., horizontal; Rt., right.

were removed, exposing the midbrain. Stimulation of the superior colliculi resulted in prompt and equal dilatation of the pupils from about 4 mm to 7 mm. A second stimulus caused the eyes to diverge up and out and the pupils to dilate markedly. No pupillary constriction or accommodation was observed. The pattern of eye movements usually obtained from stimulation of the superior colliculi were not elicited during this experiment.

Stimulation just rostral to the superior colliculi in the pretectal area resulted in bilateral and equal pupillary constriction from 6 mm to 2 mm. Accommodation was noted as manifested by a prompt change in the retinoscopic reflex (from a "with" to an "against" movement). The pupillary constriction was of shorter duration than the accommodation; that is, the pupils dilated before the retinoscopic image indicated the end of accommodation. On one occasion, stimulation produced a symmetrical convergence movement of about 10 degrees with pupillary constriction. With another stimulus, the eyes moved down and to the left at the same time that the pupils underwent constriction.

Experiment no. 13 (table 2, monkey 114). The areas stimulated in the left frontal cortex above and below the principal fissure are indicated in figure 4. Stimulation of points A in the region of the arcuate sulcus resulted in lid closure associated with pupillary dilatation. In this region there was bilateral and equal partial lid closure associated with bilateral and equal pupillary dilatation. Stimulation of nearby points elicited unilateral partial lid closure and unilateral pupillary dilatation, occasionally associated with sneering movements of the face on the homolateral or the contralateral side, or both.

More rostral to the above area, stimulation at point B resulted in conjugate deviation of the eyes to the right and at point C to the right and downward. These conjugate deviations were associated with dilatation of the pupil. On some occasions, the dilatation of the contralateral pupil was greater than of the homolateral pupil.

Stimulation of point D in figure 4 produced a divergence movement. This consisted of abduction in the contralateral eye with no movement noted in the homo-

lateral eye. Slight pupillary dilatation accompanied this ocular movement.

Stimulation still more rostrally produced bilateral and equal pupillary constriction usually associated with convergence movements. These convergence movements were of small amplitude (estimated at 5°) and the greater adduction was in the contralateral eye. Pupillary constriction was elicited without ocular movement on two occasions. Since there was no reversal of the retinoscopic reflex, accommodation was assumed not to have taken place.

Experiment no. 14 (table 2, monkey 115). The left frontal and the right occipital cortices were exposed. Stimulation beneath the midportion of the principal fissure at point A, in figure 5, produced convergence movements, usually associated with pupillary constriction. There was bilateral adduction, that was marked in the contralateral eye and slight in the homolateral eye. Further stimulation resulted in unilateral adduction in the contralateral eye with the homolateral eye remaining in the straight ahead or primary position. The pupillary constriction was bilateral and equal from about 6 mm to 5 mm. No accommodation was observed as manifested by a reversal of the retinoscopic reflex.

Stimulation of point B in figure 5 resulted in horizontal conjugate deviation of the eyes to the contralateral side associated with bilateral pupillary dilatation, that was greater in the contralateral eye. The abduction in the contralateral eye was more rapid and of greater amplitude than the adduction in the homolateral eye. Stimulation still more caudally, at point C in figure 5, resulted in a conjugate deviation of the eyes to the opposite side, that was of equal amplitude and velocity in the two eyes. There was an associated bilateral and equal slight pupillary dilatation.

Stimulation in the superior temporal gyrus, just rostral to the superior temporal sulcus (at point D in fig. 5), resulted in convergence of the eyes and pupillary constriction. The convergence movements consisted of bilateral adduction, greater in the homolateral eye than in the contralateral eye; and in unilateral adduction in the homolateral eye with the contralateral

eye remaining in the straight ahead position. The pupillary constriction associated with the convergence movements was at first bilateral and equal. However, repeated stimulation resulted in a definite anisocoria, with the homolateral pupil (measuring about 4 mm) smaller than the contralateral pupil (measuring about 6 mm). The anisocoria persisted during the remainder of the experiment and reversed itself when the animal recovered from the

anesthesia. For the first post-operative day the homolateral pupil remained slightly larger than the contralateral pupil. By the second post-operative day, the pupils were equal.

Stimulation behind the above area (at point E in fig. 5) and caudal to the superior temporal gyrus produced convergence movements and pupillary constriction similar to that described above. No accommodation was apparent, since there was

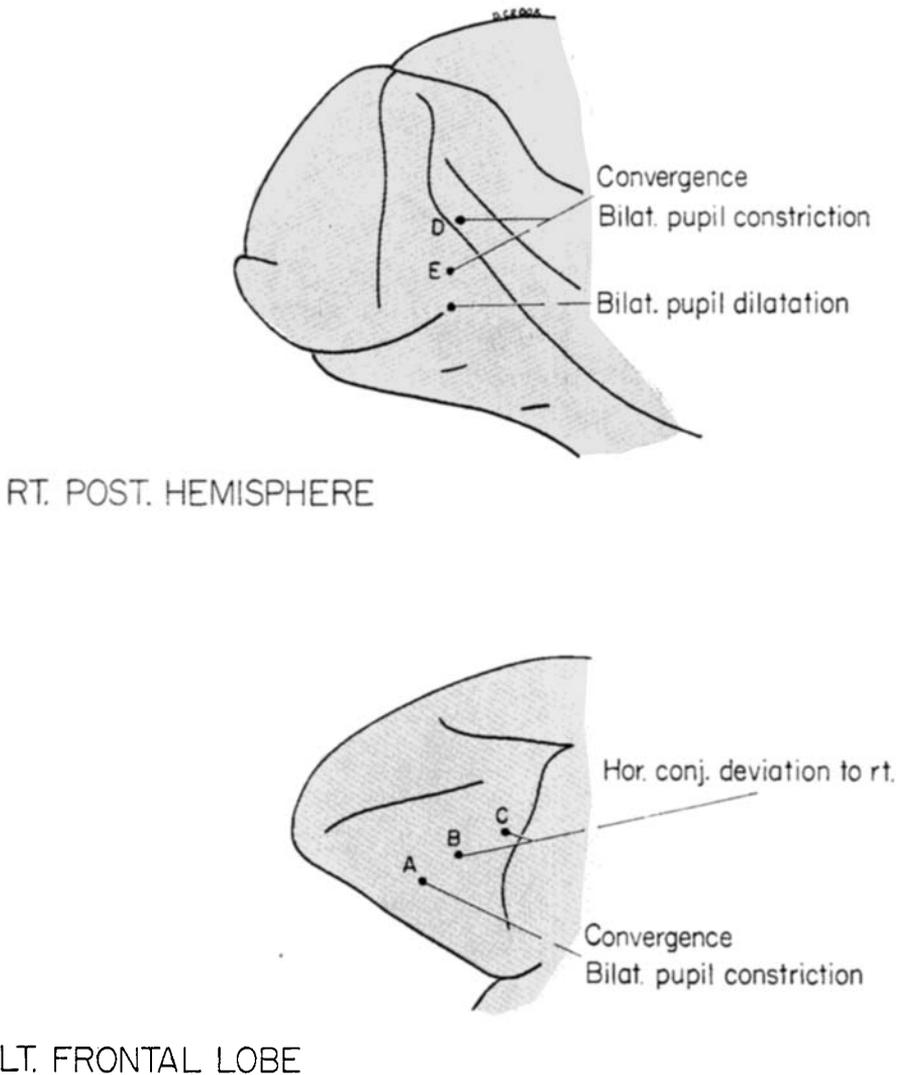


Fig. 5 A drawing of the right and left cerebral hemispheres of *Macaca mulatta* illustrating the findings in experiment 14 in monkey no. 115. Bilat., bilateral; conj., conjugate; hor., horizontal; Rt., right.

no reversal of the retinoscopic reflex. Stimulation ventral to the above area (fig. 5), and just rostral to the tip of the external calcarine sulcus, produced bilateral and equal slight pupillary dilatation (about 1 mm) unassociated with movement of the eyes.

ANATOMICAL FINDINGS

The courses of the degenerated fibers from the frontal and occipital eye fields as revealed by Marchi preparations confirm the previous work of Crosby and Henderson ('48), Crosby, Yoss and Henderson ('52), and Crosby ('56). These papers should be consulted for detailed descriptions.

From area 8 of Brodmann and the additional frontal eye field (areas 9 and 10 of Brodmann) degenerated fibers were traced from the lesions to the region of the eye muscle nuclei. These fibers pass through the internal capsule into the medial half of the cerebral peduncle. In the midbrain they could be traced bilaterally to the region of the oculomotor complex and homolaterally to the neighborhood of the trochlear nucleus. In the pons, some fibers terminate, chiefly contralaterally, in the region of the abducens complex. Through midbrain and pons some fascicles join the medial lemniscus and proceed caudally in it to the area of the contralateral abducens and parabducens nuclei.

The degenerated fibers from the lesions in the occipital and preoccipital eye fields (areas 18 and 19 of Brodmann) were traced along the visual radiations into the internal capsule. These fibers then cross the pulvinar to end deep within the superior colliculus or ventral to it in the tectum.

CONSIDERATION OF EXPERIMENTAL RESULTS

This series of experiments was designed to explore the cortical processes involved in convergence and divergence, pupillary constriction, and accommodation. In only one experiment was attention directed to the midbrain. The previous work of Crosby and Henderson ('48), Crosby, Yoss and Henderson ('52) and many others gave reason to investigate certain cortical areas, and attention was directed immediately to the frontal and the occipital eye fields.

Faradic stimulations were carried out particularly in areas 8, 9, and 10 of Brodmann in the frontal eye field and in areas 19 and 22 of Brodmann in the transition area between the temporal and the occipital lobes. These stimulations produced the majority of the results discussed below. The areas investigated are outlined and depicted in figure 6 and figure 7. However, both frontal and occipital eye fields were explored extensively confirming the previous work of Crosby and Henderson ('48), Crosby, Yoss and Henderson ('52), and Crosby ('53) and others on conjugate eye movements. Moreover, attention was paid to the relation of pupillary activity to the conjugate eye movements and to the cortical processes associated with pupillary dilatation. Other phenomena related to the eyes were also noted.

The concept of functional instability of cortical points applies to these experiments (Leyton and Sherrington, '17). Stimulation of the same cortical point may result in different responses depending upon many variables such as the strength and duration of the initial stimulus, the length of time between stimuli and the type and the depth of the anesthesia. The local temperature, the exposure, and the drying of the cortex, inadvertent trauma and compromise of blood supply, and individual differences in the experimental subject (such as temperament, age, and state of health) may also influence the results. In the study of eye movements, the type and the depth of the anesthesia have proven to be of particular importance (Crosby and Henderson, '48). It is necessary to use ether and to maintain the monkey at a level of consciousness just below the point where voluntary ocular movements are obtained and where the blink reflex to stimulation of the cilia is still retained (Henderson, '49). Light ether anesthesia causes pupillary dilatation (about 1 to 2 mm), but does not obliterate pupillary reactions. Also, every attempt was made to perform the operation quickly, since the longer the animal was under anesthesia, the more difficult it was to obtain ocular movements and the greater the danger that the cortex might become traumatized and edematous. This is illustrated in experiment 10. The monkey had a prolonged anesthesia and his cortex was

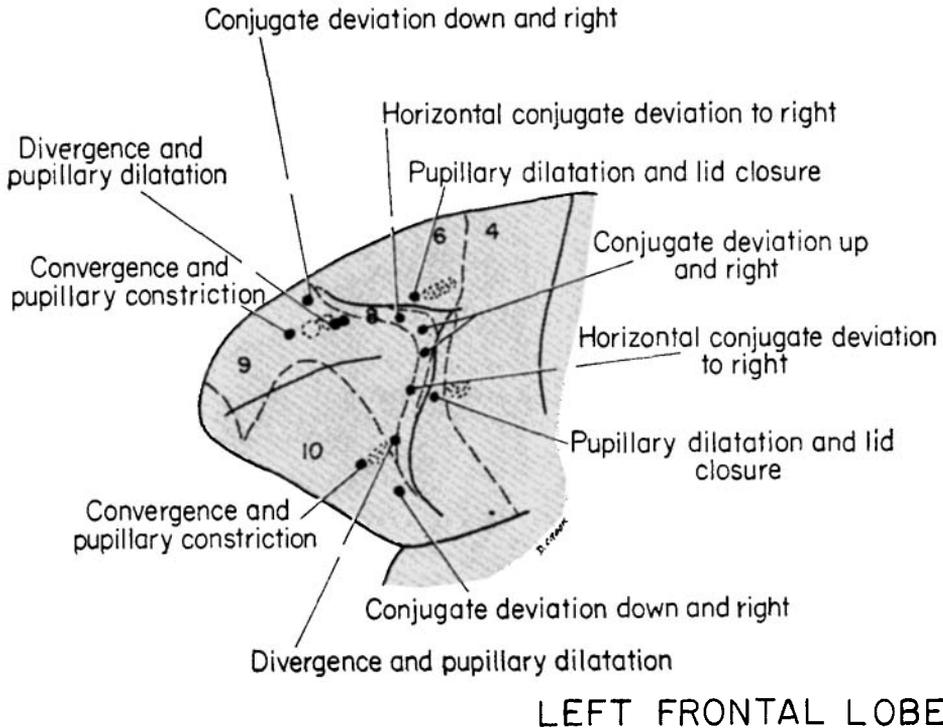


Fig. 6 A drawing of the left frontal eye field of *Macaca mulatta* summarizing the experimental findings (see text).

hyperemic and edematous. Ocular movements were obtained with difficulty and only by greatly increasing the strength of the stimulus. Bilateral pupillary dilatation was the only response elicited from large areas of the occipital eye field (fig. 4).

The first few stimuli applied to a cortical area usually proved to be the most productive. Repeated faradic stimuli applied in one area, especially if the stimuli followed each other closely, frequently failed to elicit the same response. For example, in one case, stimulation in the frontal cortex resulted in convergence movements. Repeated stimulation in that area reversed the effect and divergence movements resulted. In spite of this variability, faradic stimulation in the cortical areas described gave definite patterns of response (fig. 6 and fig. 7).

The terms convergence and divergence usually imply a bilaterally symmetrical movement of the eyeballs in which the visual axes approached each other to inter-

sect at a near point, or move apart again for more distant fixation. For our purpose, a broader definition is employed. That is, convergence is a movement of the eyes or eye so that the lines of sight in the horizontal plane meet at a point in front of the eyes. Divergence is a movement of the eyes or eye in which the lines of sight in the horizontal plane meet at a point behind the eyes. This definition includes asymmetrical movements and ductions (unilateral eye movements). It also embraces bilateral movements towards one side in which the amplitude or velocity of movement in one eye is greater than in the other, since the lines of sight of the eyes, in this case, at some time during the movement meet at a point behind or in front of the eyes.

In the frontal cortex of the macaque (fig. 6), convergence was obtained by unilateral faradic stimulation in areas 9 and 10 of Brodmann (Bonin and Bailey, '47) both above and below the midpoint of the principal fissure. In the occipital region,

they were elicited in the temporo-occipital transition zone in areas 19 and 22 of Brodmann, as illustrated in figure 7.

The convergence movements observed in these experiments can be arbitrarily divided into 4 types, with the understanding that no clear line of separation exists among them. The first type consists of a bilateral symmetrical adduction of the two eyeballs. This occurred rarely in this series of experiments and the amplitudes of the movements were slight. The second type was an asymmetrical convergence movement or bilateral adduction (inward movement) of both eyeballs in which the greater amplitude of movement was noted in either the homolateral or the contralateral eye. The amplitude of movement was never greater than about 15 degrees in one eye and 5 degrees in the other. Stimulation in the frontal cortex tended to produce the greater adduction in the contralateral eye and excitation of the temporo-occipital transition cortex, in the homolateral eye. The third type was unilateral adduction which took place in one eye with the other eye remaining in the straight ahead or primary position. Stimulation in the frontal cortex

tended to produce adduction in the contralateral eye and excitation in the temporo-occipital transition cortex resulted in adduction in the homolateral eye. The 4th type consisted of a combination of conjugate gaze and convergence in which the amplitude or velocity (or both) of lateral movement was greater in the homolateral eye (also found in the chimpanzee by Leyton and Sherrington, '17).

The pattern for divergence movements was about the same as that for movements of convergence except that in these experiments a divergence movement, consisting of a homolateral abduction, was obtained on only one occasion from stimulation in the temporo-occipital transition area. The divergence movements obtained from stimulation in the frontal cortex (fig. 6) consisted of a rare symmetrical abduction of small amplitude, bilateral asymmetrical abduction, a unilateral abduction, and a combination of conjugate gaze and divergence in which the amplitude or velocity (or both) appeared greater in the abducting eye.

Convergence and divergence movements were always of smaller amplitude than the

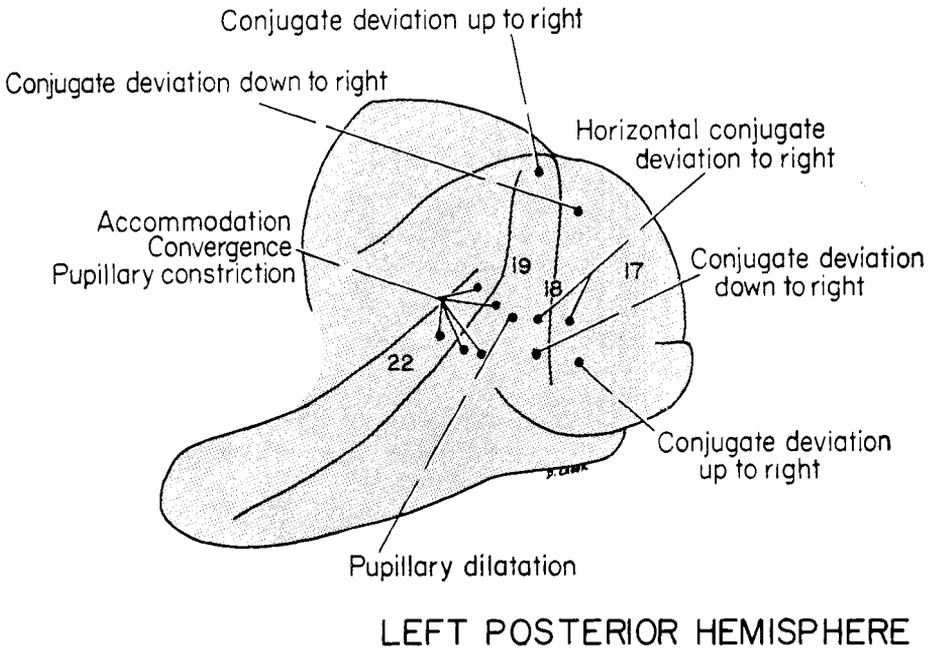


Fig. 7 A drawing of the left occipital eye field of *Macaca mulatta* summarizing the experimental findings (see text).

conjugate movements. In general, increasing the strength of the stimulation, or shifting it slightly, tended to obliterate the convergence or divergence movements and transform them into a combination of conjugate and convergence or divergence movements and then into "pure" conjugate gaze.

In the frontal cortex there appeared to be a definite pattern of response as illustrated in figure 6. Above the principal fissure, the area giving convergence on stimulation tended to be rostral and slightly *above* the area giving divergence. Below the principal fissure the area for convergence tended to be rostral and slightly *below* the area for divergence. Thus, the frontal areas related to convergence appeared distinct although they are intimately related to the areas of divergence and conjugate gaze. In one experiment performed on the midbrain in which the pretectal area was stimulated, bilateral symmetrical convergence was elicited.

Pupillary constriction in the macaque was obtained from unilateral stimulation in both the frontal and the occipital eye fields. The areas concerned overlap the areas for convergence and are illustrated in figure 6 and figure 7. The amplitude of constriction from cortical stimulation was never more than $\frac{1}{3}$ of the pupillary diameter, although stimulation in the midbrain produced pupillary constriction of more than $\frac{1}{2}$ the original pupillary diameter. The pupillary constriction noted from stimulation was usually bilateral. However, on one occasion, marked anisocoria was produced from stimulation in the temporo-occipital transition area, with the smaller pupil on the homolateral side. The pupillary constriction obtained from cortical stimulation occurred both unrelated to ocular movement and in association with convergence movements. Pupillary constriction was almost always associated with movements of convergence obtained when stimulation was in the temporo-occipital transition area. Midbrain (pretectal) stimulation resulted in marked pupillary constriction often associated with convergence and, on one occasion, with obliquely downward conjugate gaze.

Accommodation in the macaque was detected by the technique of retinoscopy

(see Material and Methods). It was obtained in 4 experiments by unilateral faradic stimulation in areas 19 and 22 of Brodmann, as depicted in figure 7. The accommodation manifested itself by a relative increase in myopia. No accommodation was noted from stimulation in area 17 of Brodmann. It is possible that a decrease in accommodation (relative increased hyperopia) may have occurred as a consequence of stimulation of these frontal and occipital areas but this could not be detected with the technique employed.

The accommodation response was associated with both pupillary constriction and convergence and with convergence alone. Both convergence and pupillary constriction were obtained as isolated phenomena, or in association with one another, without accommodation. Divergence movements were associated with pupillary dilatation or occurred as isolated phenomena.

Pupillary dilatation was elicited by unilateral faradic stimulation from both the frontal and the occipital eye fields as depicted in figures 6 and 7. It occurred as an isolated phenomenon and in association with lid closure, facial movements, divergence movements, and conjugate gaze. As an isolated phenomenon it occurred bilaterally and was of small amplitude. It was particularly evident in experiment 10 in which the brain was hyperemic and edematous. In association with lid closure, it occurred both bilaterally and unilaterally. In one instance, unilateral pupillary dilatation was produced from stimulation in the homolateral frontal cortex and was associated with homolateral facial movements, slight lid closure, and abduction of the homolateral eye. Divergence movements were not associated with pupillary constriction but frequently were accompanied by pupillary dilatation. Conjugate gaze, resulting from stimulation in the frontal eye field, was frequently associated with bilateral pupillary dilatation, more marked in the contralateral eye. Stimulation in the occipital eye field produced conjugate gaze associated with bilateral pupillary dilatation, which was more marked in the homolateral eye. Bilateral and equal pupillary dilatation, unassociated with ocular movement,

TABLE 3
Post-operative ocular abnormalities

Experiment no.	Position of lesion	Post-operative ocular findings and their duration
3	Right temporal occipital transition area	Anisocoria (right pupil 5 mm., left pupil 6 mm.); duration 8 days
6	Right frontal	Anisocoria (right pupil 4 mm., left pupil 5 mm.); duration 4 days
12	Right side of midbrain	Conjugate deviation of eyes to the left, pupils equal 5 mm.; duration about 3 hours
13	Left frontal	Anisocoria (right pupil 5 mm., left pupil 4 mm.); duration 2 days
14	Left frontal and right occipital	Anisocoria (right pupil greater than left); duration 1 day

was obtained (fig. 7) just caudal to the area in the temporo-occipital transition area related to pupillary constriction and to convergence movements.

DISCUSSION

Convergence and divergence have already been defined. The term conjugate deviation is used to describe binocular movements in which the visual axes move in parallel. However, conjugate deviation in which the eyes maintain perfect parallelism is limited to those objects fixated at infinity, i.e., for practical purposes beyond 20 feet. A large part of visual function takes place within 20 feet of the individual. In this range, binocular movements in the normal individual are combinations of conjugate deviation and convergence or divergence movements. Thus, for a large part of normal visual function, conjugate gaze and convergence or divergence movements are inseparably linked. In the experiments reported in this paper, conjugate deviations were observed in which the amplitude or velocity of movement in one eye was greater than in the other. These movements can be interpreted as combinations of conjugate gaze and convergence or divergence.

The anatomical and pathological evidence that there are separate neuronal pathways for conjugate gaze and for convergence movements at the brain stem levels has already been presented. Verhoeff ('47) emphasized physiological differences. He pointed out that, on one hand, when an eye is directed downward

and inward by the conjugate mechanism without the help of convergence, it undergoes extorsion. On the other hand, when an eye is directed downward and inward, but the inward direction is produced by the convergence mechanism, the eye undergoes intorsion. Moreover, the eye can be turned considerably farther inward by conjugate action than by convergence and, after maximum symmetrical convergence has been obtained by bifixation of an object in the midline, one eye at a time can be turned still farther inward, by carrying the fixation object to the left in case of the right eye, and to the right in case of the left eye, while bifixation is maintained. In the experiments reported here, the amplitudes of the convergence movements were always less than those of the conjugate movements.

There has been much debate and many papers have been written on the existence of so-called centers for convergence and divergence at midbrain levels. The subject is reviewed by Bruce ('35) and Adler ('53) and their discussions need not be repeated here. The word "center" has apparently been utilized to mean a region of brain substance with integrative or correlative functions which receives impulses from diverse sources. At the midbrain level the fibers subserving convergence probably lie in close proximity with, or are represented in, the cells of the oculomotor complex innervating the medial recti. Faradic stimulation in the midbrain (pretectal and tectal areas) of the macaque in one experiment resulted in symmetrical convergence movements. Such

movements have already been reported in the cat by Spiegel and Scala ('37). This fact supports the idea of a distribution and proximity of fibers (either oculomotor fibers or supranuclear tracts) to the tectum and pretectum but does not necessarily imply the existence of an integrative center.

Bilateral stimulation of corresponding points in both hemispheres has resulted occasionally in symmetrical convergence of small amplitude (Schäfer, 1888a). It is reasonable to assume that convergence is a function dependent upon both hemispheres. For example, the sensory stimuli for convergence impinge on the temporal side of the retina of each eye and impulses are transmitted to both occipital cortices (areas 17) and then, via association fibers, to the preoccipital cortices (areas 18 and 19) and the motor areas specialized for convergence movements. These areas discharge over both internal corticotectal systems to the midbrain. It is possible to visualize the transformation of asymmetrical convergence movements resulting from unilateral stimulation into symmetrical convergence movements, when corresponding areas in the two hemispheres are being simultaneously activated.

It appears, then, that the patterns for ocular movement on the macaque brain, as well as those for other complex motor activities, are formulated and integrated at the cortical level. These patterns of movement are transmitted to lower levels where they undergo adjustments and modifications dependent mainly on the individual's posture, i.e., the influence of impulses from the neck muscles, vestibular apparatus, extraocular muscles and retinas (Cogan, '56).

Divergence and unilateral abduction have been obtained by faradic stimulation in the frontal eye field, as well as from stimulation in the midbrain (the eyes turn upward and outward and the pupils dilated; see experiment 12). These responses, in addition to the recent electromyographic evidence (Breinin, '57), are further indications that divergence is a dynamic function and not merely the result of the elasticity of the external recti or of the anatomical arrangement of the orbital contents.

Although convergence and divergence movements and pupillary activity were obtained as isolated phenomena from faradic stimulation in the frontal eye field, in the usual response convergence movements were associated with pupillary constriction and divergence movements with pupillary dilatation. Conjugate gaze was usually associated with pupillary dilatation. The frontal eye fields are believed to be responsible for voluntary eye movements and, therefore, in this case, with voluntary convergence. Accommodation, manifested by a change towards relative myopia, was not observed in these experiments from stimulation in the frontal cortex.

Faradic stimulation in the preoccipital cortex resulted in accommodation, convergence movements and bilateral pupillary constriction. In every instance, in this series of experiments, accommodation was associated with convergence movements and, except on one occasion, with pupillary constriction as well. Convergence movements were obtained with pupillary constriction and without accommodation. Also, both convergence movements and pupillary constriction occurred as isolated phenomena.

The pupillary reflex to light is not dependent on the integrity of the cerebral cortex. Thus, it is assumed that the pupillary constriction resulting from cortical stimulation is related to the "near" reflex. Accommodation in the macaque was observed (apparently for the first time) from stimulation of the preoccipital cortex, and on one occasion of midbrain areas. Therefore, the three components of the "near" reflex — accommodation, convergence and pupillary constriction—are apparently represented in the preoccipital cortex in overlapping cerebral areas.

It is interesting to speculate, in the light of these experimental results, about the meaning of the convergence movements obtained from the occipital eye field. Accommodation was in every instance associated with convergence. Is this the correlate of the so-called accommodative-convergence, i.e., the convergence inseparably linked with accommodation (Alpern and Ellen, '56). Convergence was obtained associated with pupillary constriction and

without accommodation. Convergence was also obtained when neither pupillary constriction nor accommodation occurred. Are these the correlates for the so-called fusional convergence, i.e., the convergence associated with the fusion reflex (Alpern, '57)? Fusional convergence has been noted with or without pupillary constriction (Knoll, '49).

Finally, the following are left for speculation. The first is the observation that adduction resulting from stimulation in the frontal eye field tends to be of greater amplitude in the contralateral eye, but adduction resulting from stimulation in the occipital field tends to be of greater amplitude in the homolateral eye. Secondly, why, in pupillary dilatation associated with conjugate deviation to the opposite side due to stimulation of the frontal eye field, does the contralateral pupil usually dilate more than the homolateral pupil? In the occipital field it is the homolateral pupil that tends to dilate more than the contralateral pupil. Thirdly, does the fact that unequal and disjunctive eye movements are readily obtained from faradic stimulation of the cerebral cortex conflict with Hering's Law (Adler, '53)?

SUMMARY

1. Convergence and divergence movements of the eyes can be elicited by faradic stimulation in the frontal cortex of *Macaca mulatta*. The work of Crosby, Yoss and Henderson ('52) on the pattern of conjugate eye movements in the frontal eye field is confirmed (fig. 6).

2. In the transition area between the occipital and temporal cortices (areas 19 and 22 of Brodmann), faradic stimulation resulted in accommodation, pupillary constriction, and convergence—the three components of the "near" reflex (fig. 7). Accommodation was usually associated with convergence and pupillary constriction. Convergence and pupillary constriction occurred in association without accommodation or as isolated phenomena. Stimulation more caudally (in areas 18 and 19 of Brodmann) confirmed the work of Crosby and Henderson ('48) on the pattern of conjugate eye movements in the preoccipital and occipital eye fields (fig. 7).

3. The convergence movements were of 4 types: symmetrical bilateral adduction, asymmetrical bilateral adduction, unilateral adduction, and a combination of convergence and conjugate gaze, characterized by a deviation of both eyes to the opposite side, in which the adducting eye homolateral to the cortical stimulation underwent a movement of greater amplitude than did the abducting contralateral eye. These ocular movements were obtained in both the frontal and the occipital eye fields and were usually associated with pupillary constriction.

4. The divergence movements were of 4 types: symmetrical bilateral abduction, asymmetrical bilateral abduction, unilateral abduction, and a deviation of the eyes to the side opposite, with the abducting eye contralateral to the cortical stimulation showing a movement of greater amplitude than did the adducting homolateral eye. Except on one occasion, no divergence movements were noted from stimulation in the occipital eye field. Divergence movements were usually associated with bilateral and equal pupillary dilatation.

5. Conjugate deviation of the eyes was frequently associated with bilateral pupillary dilatation—usually greater in the contralateral eye, when the frontal eye field was stimulated, and in the homolateral eye when the occipital eye field was stimulated. Pupillary dilatation in one eye was noted on one occasion from homolateral frontal stimulation. Anisocoria was produced on one occasion from occipital stimulation.

ACKNOWLEDGMENTS

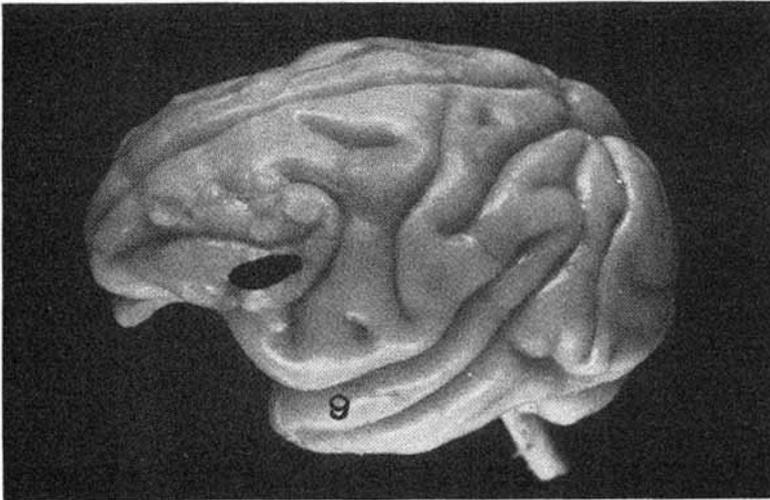
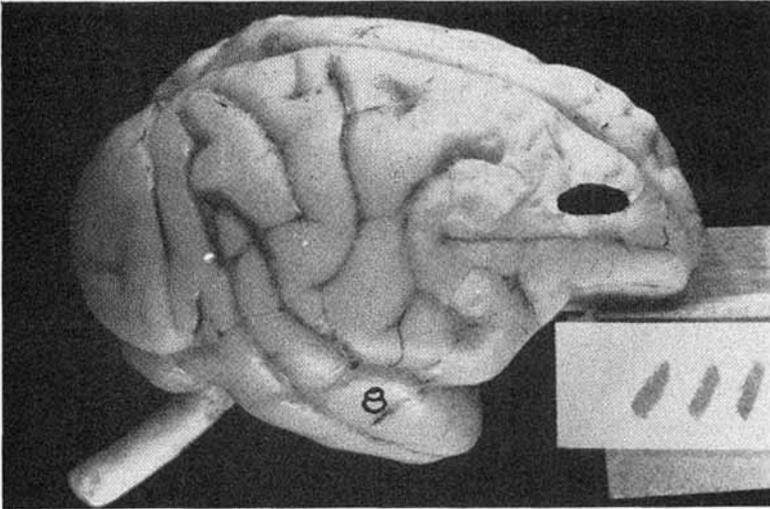
The author wishes to express his gratitude to Dr. Elizabeth C. Crosby of the Department of Anatomy, University of Michigan, and to Dr. John Henderson of the Department of Ophthalmology, University of Michigan, whose assistance and encouragement made this work possible.

LITERATURE CITED

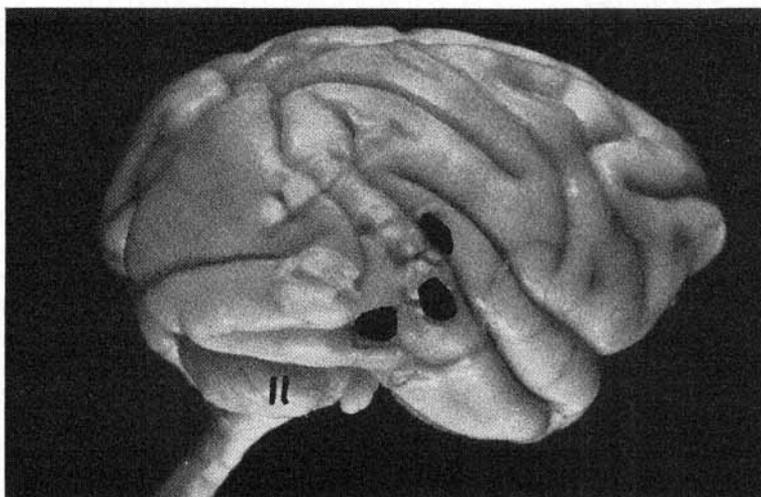
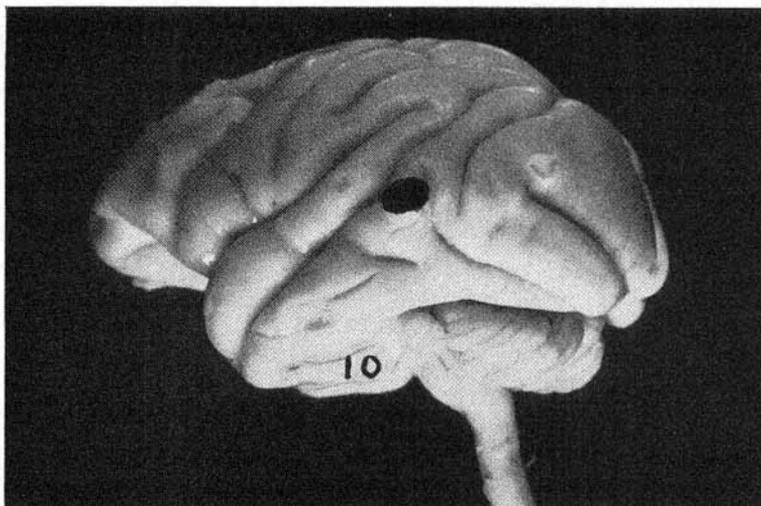
- Adler, F. H. 1953 *Physiology of the Eye, Clinical Application*. C. V. Mosby Co., St. Louis.
 Allen, M. J. 1950 The response of the intraocular muscles of the dog and cat to electrical stimulation. *Am. J. Optometr.*, 27: 287-293.
 Alpern, M. 1957 The position of the eyes during prism vergence. *Arch. Opth.*, 57: 345-353.

- Alpern, M., and P. Ellen 1956 A quantitative analysis of the horizontal movements of the eyes in the experiments of Johannes Mueller. *Am. J. Ophthalm.*, 42: 289-296.
- Barris, R. W. 1935 Disposition of fibers of retinal origin in the lateral geniculate body; course and termination of fibers of optic system of cat. *Arch. Ophthalm.*, 14: 61-70.
- 1936 A pupillo-constriction area in the cerebral cortex of the cat and its relationship to the pretectal area. *J. Comp. Neur.*, 63: 353-368.
- Barris, R. W., W. R. Ingram and S. W. Ranson 1935 Optic connections of the diencephalon and midbrain of the cat. *Ibid.*, 62: 117-153.
- Beattie, J., G. R. Brow and C. N. H. Long 1930 Physiological and anatomical evidence for existence of nerve tracts connecting hypothalamus with spinal sympathetic centers. *Proc. Roy. Soc., B.*, 106: 253-275.
- Beattie, J., A. B. Duell and C. Ballance 1932 The effects of stimulation of hypothalamic pupillo-dilator center after successful anastomoses between cervical sympathetic and certain motor nerves. *J. Anat.*, 66: 283-299.
- Bender, M. B., and N. Savitsky 1940 Paralysis of divergence. *Arch. Ophthalm.*, 23: 1046-1051.
- Bender, M. B., and E. A. Weinstein 1943 Functional representation in the oculomotor and trochlear nuclei. *Arch. Neur. Psychiat.*, 49: 98-106.
- Bonin, G. V., and P. Bailey 1947 Neocortex of *Macaca mulatta*. Ill. Monographs in Med. Sciences, 5. Univ. of Illinois Press, Urbana.
- Breinin, G. M. 1957 The nature of vergence revealed by electromyography. *Arch. Ophthalm.*, 58: 623-631.
- Bruce, G. M. 1935 Ocular divergence: its physiology and pathology. *Arch. Ophthalm.*, 13: 639-660.
- Claes, E. 1939a Contribution à l'étude, physiologique de la fonction visuelle. II. Etude des centres oculomoteur corticaux chez le chat non-anesthésié. *Arch. Int. Physiol.*, 48: 238-260.
- 1939b Contribution à l'étude physiologique de la fonction visuelle. III. Activités pupillo-motrices du diencephale et du mésentéphale chez le chat non-anesthésié. *Ibid.*, 48: 261-280.
- Clark, S. L. 1937 Innervation of the intrinsic muscles of the eye of the cat. *J. Comp. Neur.*, 66: 307-325.
- Cogan, D. G. 1937 Accommodation and the autonomic nervous system. *Arch. Ophthalm.*, 18: 739-766.
- 1956 *Neurology of the Ocular Muscles*. Charles C Thomas, Springfield, Ill.
- Crosby, E. C. 1956 The role of the midbrain as a part of the discharge path from higher centers. *Progress in Neurobiology*, 1: 217-231.
- Crosby, E. C., and J. W. Henderson 1948 The mammalian midbrain and isthmus regions; fiber connections of the superior colliculus; pathways concerned in automatic eye movements. *J. Comp. Neur.*, 88: 53-91.
- Crosby, E. C., and R. T. Woodburne 1943 The nuclear pattern of the nontectal portions of the midbrain and isthmus in primates. *Ibid.*, 78: 441-482.
- Crosby, E. C., R. E. Yoss, and J. W. Henderson 1952 The mammalian midbrain and isthmus regions; the fiber connections; the pattern for eye movements on the frontal eye field and the discharge of specific portions of this field to and through midbrain levels. *Ibid.*, 97: 357-383.
- Crouch, R. L. 1936 The efferent fibers of the Edinger-Westphal nucleus. *Ibid.*, 64: 365-373.
- Feigenbaum, A., and W. Kornbleuth 1946 Paralysis of convergence with bilateral ring scotoma following injury to the occipital regions. *Arch. Ophthalm.*, 35: 218-226.
- Foerster, O. 1928 Zur Pupillarinnervation. *Deutsche Ztschr. Nervenheilk.*, 106: 311.
- Foerster, O., O. Gagel and W. Mahoney 1936 Ueber die Anatomie, Physiologie und Pathologie der Pupillarinnervation. *Verhandl. Deutsch. Gesellsch. Inn. Med.*, 48: 386-398.
- Givner, I. 1939 Episcleral ganglion cells. *Arch. Ophthalm.*, 22: 82-88.
- Hare, W. K., H. W. Magoun and S. W. Ranson 1935 Pathways for pupillary constriction; location of synapses in the path for pupillary light reflex and of constrictor fibers of cortical origin. *Arch. Neur. Psychiat.*, 34: 1188-1194.
- Harris, A. J., R. Hodes and H. Magoun 1944 The efferent path of the dilator reflex in the cat. *J. Neurophysiol.*, 7: 231-243.
- Henderson, J. W. 1949 The anatomic basis for certain reflex and automatic eye movements. *Am. J. Ophthalm.*, 32: 232-237.
- Hensen, V., and C. Völckers 1878 Über den Ursprung der Accommodationsnerven, nebst Bemerkungen über die Function der Wurzeln des nervus oculomotorius. *Physiologische Untersuchung. Arch. Ophthalm.*, 24: 1-26.
- Hodes, R. 1940 The efferent pathway for reflex pupillo-motor activity. *Am. J. Physiol.*, 131: 144-155.
- Hodes, R., and H. W. Magoun 1942a Autonomic responses to electrical stimulation of the fore-brain and midbrain with special reference to the pupil. *J. Comp. Neur.*, 76: 169-190.
- 1942b Pupillary and other responses from stimulation of the frontal cortex and basal telencephalon of the cat. *Ibid.*, 76: 461-473.
- Holmes, G. 1918 Disturbance of vision by cerebral lesions. *Brit. J. Ophthalm.*, 2: 353-384.
- Ingram, W. R., S. W. Ranson and F. I. Hannett 1931 Pupillary dilatation produced by direct stimulation of the tegmentum of the brain stem. *Am. J. Physiol.*, 98: 687-691.
- Johnson, V. 1935 The physiologic optics of retinoscopy. *Arch. Ophthalm.*, 13: 65-70.
- Karplus, J. P., and A. Kriedl 1910 Gehirn und Sympathicus. II. Ein Sympathicuszentrum in Zwischenhirn. *Arch. Ges. Physiol.*, 135: 401-416.
- Keller, A. D. 1944 An intense and enduring miosis following transection of the brain stem, caudal to the level of exit of the oculomotor nerves. *Fed. Proc.*, 3: 23.
- Knoll, H. A. 1949 Pupillary change associated with accommodation and convergence. *Am. J. Optometr.*, Monograph 73: 1-12.
- Kuntz, A. 1953 *The Autonomic Nervous System*. Lee and Febiger, Phila.

- Kuntz, A., and C. A. Richins 1946 Reflex pupilodilator mechanisms; an experimental analysis. *J. Neurophysiol.*, 9: 1-7.
- Kuntz, A., C. A. Richins and E. J. Casey 1946 Reflex control of the ciliary muscle. *Ibid.*, 9: 445-451.
- Lashley, K. S. 1934 The mechanism of vision; the projections of the retina upon the primary optic centers in the rat. *J. Comp. Neur.*, 59: 341-373.
- Leyton, A. S. F., and C. S. Sherrington 1917 Observations on the excitable cortex of the chimpanzee, orangutan, and gorilla. *Quart. J. Exp. Physiol.*, 11: 135-222.
- Magoun, H. W., R. Atlas, W. K. Hare and S. W. Ranson 1936 The afferent path of the pupillary light reflex in the monkey. *Brain*, 59: 234-249.
- Magoun, H. W., and S. W. Ranson 1935 The central paths of the light reflex; a study of the effect of lesions. *Arch. Ophthalm.*, 13: 791-811.
- Marg, E. 1954 Accommodative response of the eye to electrical stimulation of the ciliary ganglion in cats. *Am. J. Optometr.*, 31: 127-136.
- Marg, E., J. L. Reeves and W. E. Wendt 1955 Accommodative response of the cat's eye to electrical stimulation of the ciliary ganglion. WADC Technical Report. 54-508.
- Morgan, M. W., Jr., J. M. D. Olmsted and W. G. Watrous 1940 Sympathetic action in accommodation for far vision. *Am. J. Physiol.*, 128: 588-591.
- Mott, F. W., and E. A. Schäfer 1890 On associated eye movements produced by cortical faradization of the monkey's brain. *Brain*, 13: 165-173.
- Nathan, P. W., and J. W. A. Turner 1942 The efferent pathway for pupillary contraction. *Ibid.*, 65: 343-351.
- Olmsted, J. M. D. 1944 The role of the autonomic nervous system in accommodation for far and near vision. *J. Nerv. and Ment. Dis.*, 99: 794-798.
- Parsons, J. H. 1901 On dilatation of the pupil from stimulation of the cortex cerebri. *J. Physiol.*, 26: 366-379.
- Ranson, S. W., and H. W. Magoun 1933a Respiratory and pupillary reactions induced by electrical stimulation of the hypothalamus. *Arch. Neur. Psychiat.*, 29: 1179-1194.
- 1933b The central path of the pupilloconstrictor reflex in response to light. *Ibid.*, 30: 1193-1204.
- Rasmussen, T., and W. Penfield 1948 Movements of head and eyes from stimulation of the human frontal cortex. *Res. Publ. Assoc. Nerv. Ment. Dis.*, 27: 346-361.
- Reese, W. S., and J. C. Yaskin 1941 Preservation of convergence with paralysis of all lateral movements in a case of intramedullary tumor of the pons. *Am. J. Ophthalm.*, 24: 544-549.
- Russel, J. S. R. 1894 An experimental investigation of eye movements. *J. Physiol.*, 17: 1-26.
- Schäfer, E. A. 1888a Experiments on the electrical excitation of the visual area of the cerebral cortex in the monkey. *Brain*, 11: 1-6.
- 1888b On electrical excitation of the occipital lobe and adjacent parts of the monkey's brain. *Proc. Roy. Soc.*, 43: 408-410.
- Speigel, E. A., and W. D. Hunsicker, Jr. 1936 The conduction of cortical impulses and the autonomic nervous system. *J. Nerv. Ment. Dis.*, 83: 252-274.
- Speigel, E. A., and N. P. Scala 1936 The cortical innervation of ocular movement. *Arch. Ophthalm.*, 16: 967-981.
- 1937 Ocular disturbances associated with experimental lesions of the mesencephalic central gray matter with special reference to vertical ocular movements. *Ibid.*, 18: 614-632.
- Speigel, E. A., and K. Takano 1929 Zur Analyse der vom Streifenhügel erhaltener Reizwirkung. *Ztschr. Ges. Neur. Psychiat.*, 118: 429-432.
- Stotler, W. A. 1937 Innervation of the intrinsic muscles of the eye: An experimental study. *Proc. Soc. Exp. Biol. Med.*, 36: 576-577.
- Sunderland, S., and E. S. R. Hughes 1946 The pupillo-constrictor pathway and nerves to the ocular muscles in man. *Brain*, 69: 301-309.
- Swank, R. L., and H. A. Davenport 1935 Chlorate-osmic formalin method for staining degenerating myelin. *Stain Tech.*, 10: 87-90.
- Ten Cate, J. 1934 Akustische und optische Reaktionen der Katzen nach teilweisen und totalen Exstirpationen des Neopalliums. *Arch. Neerl. Physiol.*, 19: 191-264.
- Vandergrift, G. W., and R. R. Losey 1922 A case of paralysis of convergence and paresis of accommodation. *Arch. Ophthalm.*, 51: 405-407.
- Verhoeff, F. H. 1947 Problems concerning convergence. *Tr. Am. Acad. Ophthalm.*, 52: 15-19.
- Waller, W. H., and R. W. Barris 1937 Pupillary inequality in the cat following experimental lesions of the occipital cortex. *Am. J. Physiol.*, 120: 144-149.
- Wang, G., T. Lu, and T. Lau 1931 Pupillary constriction from cortical stimulation. *Chinese J. Physiol.*, 5: 205-216.
- 1932 Pupillary dilatation from cortical stimulation. *Ibid.*, 6: 225-233.
- Ward, A. A., Jr., and H. L. Reed 1946 Mechanism of pupillary dilatation elicited by cortical stimulation. *J. Neurophysiol.*, 9: 329-335.
- Warwick, R. 1954 The ocular parasympathetic nerve supply and its mesencephalic sources. *J. Anat.*, 88: 71-93.
- 1955 The so-called nucleus of convergence. *Brain*, 78: 92-114.
- Weinstein, E. A., and M. B. Bender 1941 Pupilodilator reactions to sciatic and diencephalic stimulation; comparative study in cat and monkey. *J. Neurophysiol.*, 4: 44-50.
- Wolter, J. R. 1958 Personal communication concerning ganglion cells at ciliary root.



- 8 A photograph of the right hemisphere of monkey no. 111 illustrating the position of the lesion (inked in with India ink) in the frontal lobe above the cephalic end of the principal fissure.
- 9 A photograph of the left hemisphere of monkey no. 115 illustrating the position of the lesion (inked in with India ink) in the frontal lobe beneath the principal fissure.



- 10 A photograph of the left hemisphere of monkey no. 113 illustrating the position of the lesion (inked in with India ink) in the temporal-occipital transition area.
- 11 A photograph of the right hemisphere of monkey no. 115 illustrating the position of three lesions (inked in with India ink), one in the superior temporal gyrus and two in the temporal-occipital transition area.