RELATIONS OF BRAIN CENTERS TO NORMAL AND ABNORMAL EYE MOVEMENTS IN THE HORIZONTAL PLANE [1]

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SIX FIGURES

Man is a visualizing animal intimately related to his environment by the things which he sees in the world around him. His range of vision is increased by movements of the head and body and by deviations of the eyes. It seems probable that in man gaze in the horizontal plane is dominant over that in other directions, and it is such horizontal deviations which will be considered at the present time.

MOTOR NERVES FUNCTIONING IN HORIZONTAL DEVIATIONS

Under normal conditions impulses are continually passing over the motor nerves — the oculomotor, the trochlear, the abducens — which innervate the extraocular muscles, even when the eyes are looking straight ahead. Such impulses provide for the proper tonus of these muscles so that the eyes may be held steady and in place. The to-and-fro movements

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of the eyes which especially characterize aimless gaze — that is gaze which is not fixed definitely upon an object — actually have their neurologic basis in slight variations in this tonus of the muscles on opposite sides of each eyeball.

Section of all the nerves supplying the extraocular muscles related to an eyeball results in an immobile eye. Sometimes only a single muscle, as the lateral rectus, is paralyzed, in which case the uninjured medial rectus will draw the eye toward the nose producing a so-called unilateral internal, or convergent, strabismus and a consequent double vision or diplopia. The problem then arises as to where along the course of the abducens nerve, from its origin in its nucleus beneath the floor of the IVth ventricle (fig. 2) to its termination in the lateral rectus muscle, the lesion has occurred. Since, throughout its extent, the nerve lies in relation with many structures and has a long intracranial course, other neurological signs, as well as a paralysis of the lateral rectus, are needed to locate the lesion. As Sachs ('38) has pointed out, a bilateral abducens paralysis usually means involvement of the abducens nerves in or near the pons, but the problem of the precise situation of the lesion must still be solved. The questions here involved are illustrated by the following case history obtained through the courtesy of the Neurosurgical Service of University Hospital, Ann Arbor.

Case history. A 47-year-old woman was admitted to University Hospital in August, 1950, with bilateral abducens palsy and a diplopia. Three years earlier she had had a radical operation for cancer of the breast. Other than headache and occasional attacks of vertigo there were no localizing neurological signs. The otological examination was negative. The x-ray and electroencephalographic studies and a ventriculogram gave no indication of the site of the lesion. She had no Babinski reflex and the Romberg signs were normal. The likelihood of a brain tumor or of an aneurysm was considered but, since a distantly placed, space-occupying growth may exert pressure upon the abducens nerves during their long intracranial course, the bilateral internal strabismus alone was insufficient for localizing the lesion. The patient was dismissed from the hospital with a diagnosis of bilateral abducens nerve palsy of undetermined origin.

Fig 1 The bilateral internal strabismus should be noted.

In November, 1950, she reentered the hospital. The internal strabismus (fig. 1) was, if anything, more marked, the headaches were increased, and she had had one episode of unconsciousness which had lasted several hours. Neurological examination revealed increased deep reflexes at both ankles and knees and a bilateral Babinski sign, suggesting a beginning involvement of the portions of the pyramidal systems related to the voluntary movements of the legs and the feet. Preparatory to operation an arteriogram of the vertebral artery was made; it indicated some type of space-occupying lesion at the base of the pons near the midline.

The patient died before an operation could be performed. Postmortem examination showed an adenocarcinoma (probably metastatic from the breast carcinoma) infiltrating both abducens nerves and pressing upon the base of the pons. Recent hemorrhages had involved the most ventral fascicles of the pyramidal systems.

The case just discussed indicates that here the most ventral bundles of the pyramidal systems are concerned with mediating impulses related to voluntary control of the distal part of the lower extremities; it emphasizes the relations of the abducens nerves to such fascicles of these systems near the points of emergence of these nerves from the pons.

CONJUGATE HORIZONTAL DEVIATIONS

It is not possible for the normal individual to turn one eye lateralward without turning the other eye toward the nose. Such simultaneous movement of both eyes in a given direction is known as conjugate deviation. In order to produce such conjugate deviation in the horizontal plane, the lateral rectus of one eye and the medial rectus of the other must contract simultaneously, as their opposing muscles relax.

In the reticular gray adjacent to the abducens nucleus and intermingled with the abducens neurons are small associative cells which constitute the parabducens nucleus (Strong and

Elwyn, '48) and which send their processes forward through the brainstem. Opinions differ as to whether the fibers cross at once, after their origin in the parabducens nucleus, and ascend in the contralateral medial longitudinal fasciculus in man (Cogan, Kubik and Smith, '50), or whether the fibers related to such conjugate deviation (whether from parabducens nucleus or vestibular gray) ascend in the fasciculus

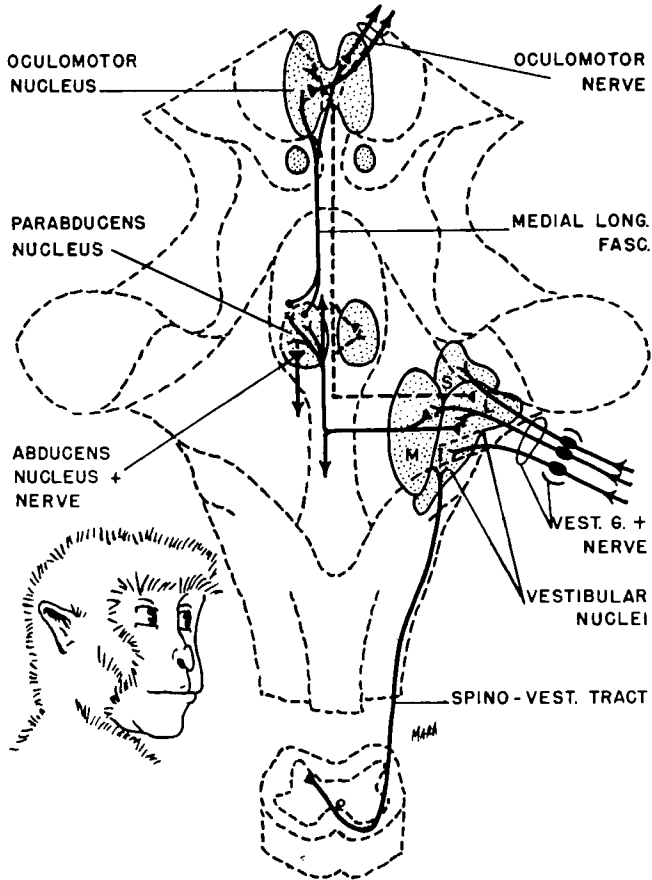Fig. 2 A diagram showing some connections of the vestibular system related to horizontal conjugate deviation of the eyes.

I, inferior vestibular nucleus; L, lateral vestibular nucleus; M, medial vestibular nucleus; MEDIAL LONG. FASC., medial longitudinal fasciculus; S, superior vestibular nucleus; SPINO-VEST. TRACT, spino-vestibular tract; VEST. G. + NERVE, vestibular ganglion + vestibular nerve.

on the side of the deviation (Spiegel and Sommer, '44; Grinker and Bucy, '49; Crosby, '50; Cranmer, '51; and others) and then decussate in part within the oculomotor nucleus (fig. 2). In any case such fibers end around those cells of origin of the oculomotor nerve which supply the medial rectus muscle of the opposite eye. Thus simultaneous contraction of the lateral rectus of one eye and the medial rectus of the other becomes possible. Since the forward-extending pathway is a component of the medial longitudinal fasciculus, bilateral destruction of this fasciculus produces a discoordination in conjugate deviation of the eyes toward either side, a condition known clinically as bilateral internuclear ophthalmoplegia.

VESTIBULAR ARCS RELATED TO HORIZONTAL DEVIATION

The simple neuron arcs just described as underlying horizontal conjugate deviation become the final common path for impulses from various centers of the brainstem, the cerebellum, and the cerebral cortex. Among such brainstem centers are those of the vestibular system, the peripheral organs of which are the semicircular canals, set in the three planes of movement of the head, and other specialized macular epithelium of the internal ear. With changes in position of the body and the head, the eyes likewise shift. Thus in automatic gaze, when the head is turned to the right, the eyes deviate toward the left; if the head is bent downward, the eyes are directed upward; if it is tilted backward, the eyes deviate downward. These are the so-called compensatory eye movements which "have been known in antiquity" (Lorente de Nó, '32, p. 233) and have been repeatedly studied. Changes in eye position in the horizontal direction may be initiated by impulses set up in the ampullary end of each lateral semicircular canal. These impulses are relayed over each vestibular nerve, with cells of origin in each vestibular ganglion, to the homolateral vestibular areas of the brainstem and to the cerebellum (Spitzer, '24; and many others).

It is usual to regard vestibular fibers in mammals (fig. 2) as terminating in all the vestibular nuclei and the cerebellum (Gray, '26, cat; Ariëns Kappers, Huber and Crosby, '36, mammals; Krieg, '42, mammals; Spiegel and Sommer, '44, man; Grinker and Bucy, '49, man; and others), yet the actual details of such termination in the lateral vestibular nucleus need further documentation. Although the vestibular root fibers are easily traced through the lateral vestibular nucleus, some observers have been unable to demonstrate endings of such fibers in relation with its constituent neurons. Winkler ('18, rabbit) described the vestibular root fibers relaying impulses by way of intercalated neurons to the large cells of Deiters' nucleus. Spitzer ('24, man) and Spiegel and Sommer ('44, man) thought that connections were made by collaterals of the root fibers with the cells of Deiters' gray. Certainly, either directly or indirectly, impulses entering over the vestibular nerves are relayed to the lateral vestibular nuclei as well as to the other vestibular nuclei and the cerebellum. Winkler ('18) described a wide distribution of such fibers including some to the abducens nucleus.

Opinions differ, also, as to the precise location within the vestibular area of the neurons which discharge ascending fibers to the medial longitudinal fasciculus. There is fairly general agreement that each superior vestibular nucleus contributes fibers to the homolateral ascending fasciculus. Frequently (Rasmussen, '32, cat; Ranson and Clark, '47, man; and many others) these fibers have been regarded as terminating in all the eye muscle nuclei. If so it seems probable that they are not excitatory — perchance they are inhibitory — to the abducens neurons since vertical deviation of the eyes appears to be obtained on excitation of the superior vestibular nucleus (Cranmer, '51, macaque; and others). From Deiters' nucleus (Ramón y Cajal, '09–'11), from Deiters' nucleus and neighboring gray (van Gehuchten, '04, rabbit), from the front end of the inferior vestibular nucleus (Spitzer, '24, man), from the medial vestibular nucleus (Gray, '26, cat; Rasmussen, '45, man; Buchanan, '51, man), from the medial

and the caudal two-thirds of the lateral vestibular nucleus
(Buchanan, '37, cat), from the lateral and medial vestibular
nuclei (Crosby, '50, man; Cranmer, '51, macaque) and from
the lateral vestibular nucleus (Fraser, '01, man; Muskens,
'14, rabbit; Winkler, '18, rabbit; and others) fibers have been
described as passing to the midline, decussating, and then
ascending in the medial longitudinal fasciculus. Some of this
disagreement as to the origin of these ascending fibers to
the abducens nucleus has its basis in differences in interpre-
tation of the caudal limits of the lateral vestibular nucleus.
If the name is applied only to the very large celled part of
this nucleus, as is sometimes done, then the fibers ascending
in the medial longitudinal fasciculus arise from the front end
of the inferior vestibular nucleus, as Spitzer ('24) stated.
If the name lateral vestibular nucleus is regarded as including
associated groups of smaller cells, then the ascending bundles
to the eye muscle nuclei arise from such groups in the caudal
two-thirds of the nucleus, as Buchanan ('37) believed. The
macaque material available for study at Michigan (which
has been reported upon by Cranmer, '51) would appear to
document connections from the medial, and the caudal two-
thirds of the lateral, vestibular nuclei, through the contra-
lateral medial longitudinal fasciculus, to the abducens nucleus
with termination there. In the abducens nucleus these fibers
end on the motor neurons of the abducens nerve, for contrac-
tion of the lateral rectus on the side of stimulation, and on
the cells of the parabducens nucleus (Strong and Elwyn, '48,
man; Cranmer, '51, macaque, man), for appropriate connec-
tions with the oculomotor nucleus for contraction of the medial
rectus of the other side, thus completing the arc for conjugate
deviation of the eyes toward the side of the contracting lateral
rectus (fig. 2).

Ascending fibers to the trochlear and oculomotor nuclei
from the contralateral medial and/or lateral vestibular nuclei
without synapse in the parabducens nucleus have been de-
scribed by many observers (Buchanan, '37, cat; Spiegel and
Sommer, '44, man, based also on study of carnivores; Ras-

mussen, '45, man; and others). From the superior vestibular nucleus fibers ascend in the homolateral medial longitudinal fasciculus to the trochlear and oculomotor nuclei and also terminate according to various observers in the homolateral abducens nucleus.

The pathways just described provide for the contraction of the eye muscles toward the side of deviation but do not explain the concomitant relaxation of the antagonistic muscles. Opinions have differed widely as to how this is accomplished, either during deviation of the eyes to the other side or in horizontal nystagmus, where there is an alternate relaxation and contraction of the muscles on the two sides of the eyeball. To discuss the various theories as to the areas involved in such relaxation and to document them properly are beyond the limitations of the present account. Reference is made to the extensive work of Lorente de Nó ('32) and to the discussion of this matter by Spiegel and Sommer ('44). The latter observers have given considerable consideration to the experimental literature and have presented, also, a theoretical application of Gesell's ideas (Gesell, '40, and elsewhere) of the way in which excitation or inhibition of impulses passing through a neuron occurs, as an explanation of reciprocal inhibition. Certainly after paralysis of the left lateral and the right medial rectus muscles stimulation of the homolateral labyrinth (Bartels, '19) or of appropriate portions of the contralateral frontal eye field (Sherrington, 1893; Crosby and Yoss, to be published) produces a return of the eyes to the midline. Such results indicate that there is more than one pathway by which such relaxation may be accomplished. It is suggested that in deviation due to vestibular stimuli, impulses may be relayed from the lateral and/or medial vestibular nuclei through ascending fibers in the homolateral medial longitudinal fasciculus (such as those figured by Spitzer, '24; Rasmussen, '45; and others) to the homolateral abducens nucleus to lessen or inhibit its discharge. Similar impulses (with or without synapse in the parabducens nucleus) might then be projected upon the cells of origin of the oculomotor

fibers supplying the contralateral medial rectus muscle. Obviously the problem needs further consideration.

Simultaneous projection of impulses from the vestibular centers on the two sides of the brain to the eye muscle nuclei tends to stabilize the incessant movements of the eyes characteristic of aimless gaze. However, since the unsupported head is rarely completely still, there is a continual slight stimulation of the vestibular nuclei, first on one side and then on the other. Consequently, there is a constant interplay between the vestibular discharge to the abducens nucleus on the right and to that on the left, so that the position of the eyes from time to time is related to the balance in discharge beween the vestibular centers on the two sides of the brain.

Actually, in aimless gaze the eyes are never at rest, although the movements are so slight as to attract no attention. Such slight movements, however, as Marx and Trendelenburg (Kestenbaum, '46) have pointed out, can be emphasized by projecting a beam of light focused on the cornea onto a scale on a distant wall, and then are very evident. When the eyes are fixed on an object such movements increase in frequency but decrease in amplitude and when the frequency has exceeded 33 to-and-fro movements per second the eyes are said to be still.

It is generally conceded that destruction of a labyrinth or of a vestibular nerve produces a nystagmus which, however, is compensated for within a few days or possibly a week (presumably by central regulation, DeJong, '50). A strongly irritating lesion within the medial and lateral vestibular areas tends to cause a deviation of the eyes away from the side of the lesion. If the irritation is not sufficiently strong or does not involve enough of the vestibular nuclei to hold the eyes in the deviated position, a slow turning of the eyes toward the other side and then a quick return to center will occur, followed by a succession of such slow deviations and quick returns. Such a vestibular nystagmus has been studied experimentally or described in various animals by many observers (as Leidler, '13, rabbit; Krieg, '42, mammals; Cran-

mer, '51, macaque) and may be a part of such clinical syndromes as that caused by thrombosis of the posterior inferior cerebellar artery (Grinker and Bucy, '49; DeJong, '50; and others). This sequence of movements constitutes a horizontal nystagmus. Since the slow component of this nystagmus is hard to see and the quick component very evident, the clinician reads the nystagmus in terms of the quick component. Thus an irritating lesion in the right medial and lateral vestibular nuclei will produce a nystagmus to the right (i.e., with its quick component to the right), the more usual type in a central vestibular lesion (Grinker and Bucy, '49). If the lesion involves the superior vestibular nucleus (and possibly the most rostral part of the lateral vestibular nucleus), the nystagmus is vertical or oblique (Cranmer, '51). If it includes much or all of the vestibular region, the nystagmus is rotatory or irregular in type. That a nystagmus may result also from an irritating lesion at upper cervical levels (probably above C4) of the spinal cord is generally recognized among neurologists (DeJong, '50; and others). The impulses thus set up ascend in the spino-vestibular pathways (fig. 2) which connect the proprioceptive centers of the cord with the inferior vestibular nuclei; within the vestibular areas there is a transference of impulses to pathways connecting with the eye muscle nuclei. Such cervical cord lesions may produce a nystagmus in the horizontal or in the vertical plane. Experimental evidence for the production of nystagmus from cervical levels is to be presented soon by Dr. Robert McCloskey. If a unilateral lesion in the lateral and medial vestibular nuclei shifts from an irritative to a destructive type, or is primarily destructive, the balance between the vestibular areas on the two sides is changed; consequently the nystagmus is reversed and/or the eyes may be deviated toward the side of the lesion.

CERTAIN CEREBELLAR ARCS INFLUENCING HORIZONTAL DEVIATION

It has been demonstrated in both embryological and phylogenetic studies of the region (Ingvar, '19; Ariëns Kappers,

Huber and Crosby, '36; Dow, '42a; Larsell, '47, '51; and elsewhere) that portions of the cerebellum grow up in intimate relation with the vestibular system and that vestibular nerve fibers (Ramón y Cajal, '09–'11, cat; Gray, '26, cat; Dow, '36, rat and cat; Rasmussen, '45, man; and others) and vestibulo-cerebellar fibers (Winkler, '18; and others) end directly within this brain center — particularly in its flocculus, uvula,
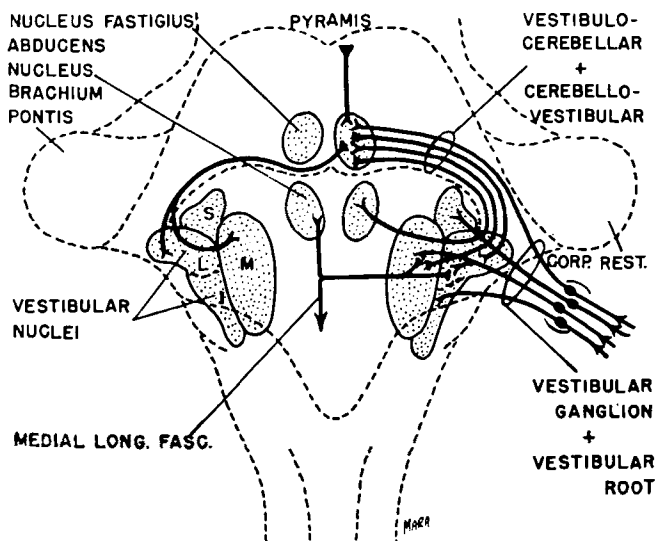

Fig. 3 A diagram of interconnections between the nucleus fastigius of the cerebellum and the vestibular centers of the brainstem related to horizontal conjugate deviation of the eyes.

CORP. REST., corpus restiforme; I, inferior vestibular nucleus; L, lateral vestibular nucleus; M, medial vestibular nucleus; MEDIAL LONG. FASC., medial longitudinal fasciculus; S, superior vestibular nucleus.

and nodule (Fulton and Dow, '37–'38, mammals; Larsell, '51, man; and others) and in its roof nuclei, the fastigial nuclei (Rasmussen, '45, man; Fulton, '49, mammals; Crosby, '50, man; and others). Therefore, it is not surprising that this suprasegmental portion of the brain exerts a direct influence over the vestibular reflex arcs. From each nucleus fastigius, cerebello-vestibular fibers (fig. 3) discharge to the homolateral lateral and medial (?) vestibular nuclei to facilitate their re-

sponses and to the contralateral lateral (and medial) vestibular nuclei to reduce or inhibit the flow of impulses through
them. Many observers (Spitzer, '24; Ariëns Kappers, Huber
and Crosby, '36, mammals and submammals; Marburg, '39,
man; Fulton, '49, mammals; and others) have described fastigio-vestibular connections. Very clear-cut evidence for the
existence of crossed and uncrossed paths from each nucleus
fastigius to the homolateral and contralateral lateral vestibular nuclei of the macaque is being presented by Rand ('52).

The dual functions of the nucleus fastigius with relation
to the vestibular centers is in line with the views of various
students of cerebellar function. Denny-Brown, Eccles and
Liddell ('28–'29) showed that either excitation or inhibition
of the action of extensor or flexor muscles may occur with
electrical stimulation of the cerebellar cortex in the vermis
portion of the anterior lobe and the median portion of the
lateral lobes. Inhibition or suppression (Snider, McCulloch
and Magoun, '49; Snider and Magoun, '49; Snider, '50) of
the activities of various centers may result from stimulation
of certain cerebellar regions. Sometimes such inhibition may
be obtained from a cerebellar area (anterior lobe) in the cat
(Sherrington, 1898; Snider and Magoun, '49) comparable to
a region which yields facilitation of reflex activity and of
movements in the monkey (Snider and Magoun, '49). Various
experiments (Sherrington, 1898; and others) have indicated
that decerebrate rigidity is lessened or suppressed following
stimulation of the anterior lobe of the cerebellum.

The facilitatory action of the cerebellum over the various
functioning brain and cord centers has been stressed by
Rossi ('13), Walker ('38), Moruzzi ('41), Snider and Magoun
('49), and many others and motor responses have been obtained from stimulation of appropriate cerebellar regions
(Mussen, '27, cat; Hampson, Harrison and Woolsey, '46,
dog, cat, monkey; and others). Snider and Magoun ('49,
monkey) described two general regions of the cerebellar cortex — an anterior and a posterior — stimulation of which
facilitates reflex activity and movements obtained from cere-

bral cortex. The anterior region falls within the anterior lobe and lobulus simplex, the posterior region within the paramedian lobule, tuber vermis, and pyramid.

In voluntary turning of the head toward either side the eyes usually deviate in the direction of the head rotation, although, of course, this response can be varied. Impulses are also discharged over cerebello-motorius fascicles (fig. 3) from the nucleus fastigius directly to the abducens nucleus (Spitzer, '24, man; Fulton and Dow, '37–'38, mammals; Fulton, '49, mammals; Rand, '52, macaque) and other motor nuclei. Such impulses make provision for adequate tonus of the eye muscles concerned in conjugate deviation of the eyes including such deviations as portions of voluntary or following responses. Concurrent with the voluntary rotation of the head toward one side (as the right) it is thought (Dow, '42b, cat and monkey; Cranmer, '51, macaque, man; Schneider, Kahn and Crosby, '51, man) that impulses reach the pyramis of the cerebellum on the right side by way of the fronto-ponto-cerebellar system from the left cerebral cortex. Such impulses inhibit the discharge of the left nucleus fastigius to the homolateral and contralateral lateral (and medial) vestibular areas. In 1939 Dow obtained action potentials in various portions of the cerebellar cortex, including the pyramid, with stimulation of the pons in the cat and, in 1942 (Dow, '42b), widespread cerebellar action potentials as a result of electrical excitation of a considerable number of cortical areas (4, 6, 8, 9, and 10 in frontal lobe, postcentral gyrus, 7, 18, 19, 21, and 22 in parietal and temporal regions in the macaque) with great projection (as judged by amplitude and threshold) to the vermian and adjoining cerebellar regions from cerebral areas adjacent to the central fissure. Also inhibitory impulses directly from cortical centers to vestibular areas are said to prevent the usual vestibular responses to caloric stimulation of the ear of macaque with cold water (Bárány, Vogt and Vogt, '23). Both types of impulse appear to the present writer to lessen the tendency of the eyes to turn away from the direction of head rotation (predominant in vestibular

reflexes) and permit them to deviate as part of the voluntary response in the direction of that rotation. Dow's results ('38, macaque) suggest that the vestibular part of the cerebellum (particularly the uvula and the nodule) exerts an inhibitory effect over the vestibular centers. Moreover, in an animal deprived of vestibular functions by bilateral labyrinthectomy, destruction of these vestibular portions of the cerebellum did not produce, at least in the immediate postoperative period, the disequilibration resulting when only the cerebellar parts were removed and the labyrinths were intact. Presumably the arcs underlying deviation of the eyes toward the side of excitation, after stimulation of the nucleus fastigius with stimuli of proper potential (Fulton and Dow, '37–'38; noted also in the Laboratory at Michigan), include both cerebello-vestibular fibers and cerebello-motorius fascicles directly to the abducens nuclei (Spitzer, '24, man; Fulton and Dow, '37, mammals; Fulton, '49, mammals; Rand, '52, macaque). Considering these various interrelations it is not surprising that lesions (such as abscesses) pressing upon one side of the posterior vermis (including the pyramis, Cranmer, '51, macaque, man; or uvula and nodule, Dow, '38, macaque), or involvements of one nucleus fastigius itself, may produce a cerebellar nystagmus present only or accentuated when the eyes are turned toward one side (or vertically). Moreover, the quick component of such a nystagmus may change in direction if a lesion shifts from suppressive to irritative (or vice versa) during the course of a syndrome (Schneider, Kahn and Crosby, '51). Dow ('38) found also that unilateral destruction of the uvula and nodule in the macaque might produce a deviation of the head away from the side of the lesion and that the inconstant horizontal nystagmus showed a quick component toward the side of the involvement.

Some of the effects of vestibular and cerebello-vestibular irritation and imbalance are illustrated in the following case history obtained through the kindness of the Neurosurgery Service at University Hospital. Those interested in the clini-

cal findings might compare this case with the one reported by Spitzer in 1899.

Case history. The patient was admitted to University Hospital on November 29, 1949, with a persistent occipital headache, bouts of vomiting (with or without nausea), and a history of one blackout spell earlier in the month and of intermittent attacks of double vision or diplopia over the last two years. He had marked papilloedema. All of these conditions suggested an increase in intracranial pressure. He walked with his feet far apart, stumbled toward either side, and showed past pointing. These are all signs of an involvement of the cerebellum or of the superior or inferior cerebellar peduncles leading to or from it. Since the patient showed no tremor on voluntary movement (a sign of lesions of the superior cerebellar peduncles), since he had no difficulty in arresting movement in one direction and substituting that in another direction (adiodokokinesis, often experienced in cerebellar hemisphere destructions), and since he fell to either side rather than backward or forward, as often occurs in vermis deficiencies, it seemed probable that the lesion included the inferior cerebellar peduncles.

There were no defects in the visual fields but, whenever the patient turned his eyes in any direction, a marked nystagmus appeared. This nystagmus in all directions of gaze suggested a bilateral imbalance in discharge of the vestibular areas. The increased intracranial pressure and the signs of bilateral vestibular and inferior cerebellar peduncle involvement pointed to a IVth ventricle tumor and this diagnosis was confirmed by a ventriculogram.

An operation was performed on December 1, 1949, by Dr. Edgar Kahn. From the floor of the IVth ventricle a tumor was removed which extended forward to block the aqueduct, spread lateralward to the middle cerebellar peduncles, and continued into the lateral recesses of the IVth ventricle into relation with the inferior cerebellar peduncles and the vestibular areas. The only apparent injury to the ventricular floor from removal of the tumor was confined to a small area in which it had infiltrated the left facial colliculus. The patient was dismissed from the hospital on December 14, 1949.

Following the operation the intracranial pressure gradually returned to normal and the cerebellar signs cleared up. However, in the area where the ventricular wall with the underlying pontine tissue was injured during operation there was some destruction of nervous tissue. A paralysis of the face on the left side — indicated by an inability to close the eye, wrinkle the forehead, or smile on that side of the face — and a deviation of the eyes to the right were evident the day after the operation. The facial palsy was due to a blocking of impulses over the motor facial rootlets as they curve around the

abducens nucleus. The irritation of the lateral and the medial vestibular areas produced a forced deviation of the eyes toward the other side.

Fig 4 The forced deviation of the eyes to the right and the evidences of a right facial paralysis should be noted.

On December 12, 11 days after the operation, the Ophthalmology Department found still a 15° to 20° deviation of the eyes to the right with the patient unable to look straight ahead. He could turn his eyes to the right, up to the right, and down to the right, though with some difficulty and with a nystagmus in the end positions, but he could not carry out these movements on the left, although he could turn the eyes almost to the midline on trying to look upward. The photograph (fig. 4) shows the deviation of the eyes; it is to be noted that this deviation is greater for the left eye than for the right. The photograph also shows signs of the still persistent facial palsy.

When the patient returned for a check-up on December 22, the facial paralysis on the left still remained but the forced deviation of the eyes to the right had disappeared. There was, however, limited movement on looking to the left (but somewhat less in looking up or down to the left) associated with a 20° to 25° left convergent strabismus. The strabismus was due, of course, to an inclusion of the abducens nucleus in the lesion, an involvement indicated earlier (and probably present from the time of the operation) by the greater deviation of the left than of the right eye during their forced turning to the right. The limitation of movement in turning either eye toward the left shows that the parabducens as well as the abducens neurons on the left were affected by the lesion. The nystagmoid movements still demonstrable, particularly on upward deviation, were thought to be the result of a persisting imbalance in discharge of the vestibular centers and cerebello-vestibular arcs.

Two other postoperative clinical signs seen in examinations of this case are of interest in evaluating the position and extent of this operative lesion although they do not deal with eye movements. One of these was a diminution of sweating on both sides of the body and a loss of sweating on the same side of the face, indicating interference with descending pathways from the hypothalamus concerned with sweating as a part of the heat regulating mechanism of the body. The other symptom was a decrease in corneal sensitivity which was still demonstrable on the last examination of the patient.

THE RÔLE OF THE MIDBRAIN IN HORIZONTAL
DEVIATIONS

Other brainstem centers usually regarded as associated with eye deviations are the superior colliculi of the midbrain. In most subprimates, these colliculi are important regions of termination of impulses set up by visual stimuli. Such impulses excited from objects above the plane of the horizon are projected on the front and medial portions of the superior colliculi, those from below the plane of the horizon on their caudal and lateral portions (Brouwer and Zeeman, '26; Brouwer, '27); impulses from the right visual field reach the opposite superior colliculus but impulses from the mid-portions of the visual fields reach the superior colliculi of both sides in many subprimates. Experimental stimulation of these midbrain areas produces a turning of the eyes in the appropriate directions including deviations in the horizontal plane. Horizontal deviation is brought about by discharge from one superior colliculus over the medial tecto-bulbar pathway to the contralateral abducens nucleus where connections are made for conjugate deviation of the eyes in the horizontal plane, toward the visual field from which the original impulse arose.

In primates, and particularly in man, there is a sharp reduction in the number of optic fibers which terminate in the superior collicular region (Crosby and Henderson, '48), only the most simple reflexes being mediated directly through this center. Clinicians recognized many years ago that destruction of the thalamic visual centers (lateral geniculate nuclei) in man eliminates eye movements in response to visual stimuli except such simple ones as blinking. Probably the visual reflexes mediated by these midbrain regions in lower animals are subordinated gradually, through the ascending mammalian scale, to those discharges to the superior colliculi from cortical centers which appear in mammals and which increase from lower to higher mammals. In primates all but the most simple visual reflexes require cortical participation in the arc. Nevertheless when the overlying occipital and parietal areas of

the cortex are removed in a macaque and midportions of the superior collicular regions exposed and stimulated, horizontal deviation of the eyes to the side opposite stimulation is obtained (Crosby and Yoss, to be published). This suggests that the pattern for discharge of visual reflexes which in subprimates is through the superior collicular region remains in primates, although it is overlaid, perhaps inhibited (for horizontal deviation of the eyes), by the activity of higher centers in the uninjured primate brain.

FOLLOWING MOVEMENTS AND OPTOKINETIC NYSTAGMUS

Obviously, simple visual reflexes such as blinking can occur in animals from which the cerebral cortex has been removed or in man even if this cortex be degenerated. However, the majority of eye deviations are either automatic or voluntary in type and depend upon arcs which include cortical relays. Automatic eye movements are stereotyped in character but may or may not involve immediate awareness. Unless inhibited voluntarily, eyes automatically follow a steadily moving object in the visual field. This is accomplished by fixing the eyes upon the moving object and keeping them centered upon it as it passes across the field, and, when the movement ceases, still directing the gaze toward it unless the eyes are turned elsewhere by a voluntary response. Children learning to read use such following movements. Individuals with frontal lobe involvements which prevent voluntary deviation of the eyes may read in the same way. Fixation and following movements are so important that special neuron arcs provide for their initiation and maintenance.

The studies of Brouwer and Zeeman ('26), Brouwer ('27), Poljak ('33), and others, which, taken together, have shown the pattern of retinal projection through the lateral geniculate nucleus and onto the visual cortex (area 17) of monkeys, are familiar to most neurologists. Impulses from the superior retinal quadrants (or inferior visual fields) are relayed to the upper portions of areas 17, those from the inferior retinal

quadrants (or superior visual fields) to the lower portions of these areas (fig. 6 A'). In man the visual radiations terminate in closer proximity to the calcarine fissure. The projection of impulses from the inferior visual fields on the superior lips of the calcarine fissures and those from the superior visual fields on the inferior lips of these fissures, with impulses from macular centers largely, if not exclusively,

EYES DOWN TO RIGHT
DIVERGENCE
DEVIATION TO RIGHT
EYES UP TO RIGHT

TO OTHER SIDE
UP TO RIGHT
UP
DOWN TO RIGHT

EYES DOWN TO RIGHT
DIVERGENCE
DEVIATION TO RIGHT

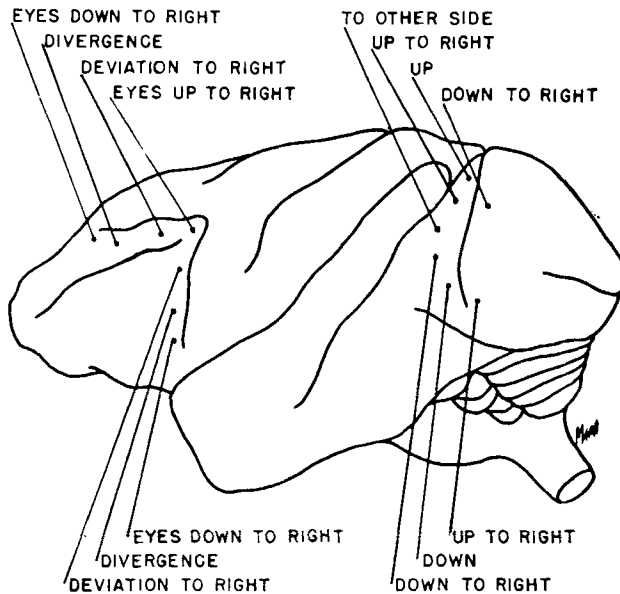UP TO RIGHT
DOWN
DOWN TO RIGHT

Fig. 5   A diagram of the left hemisphere of the macaque showing the patterns for eye deviations obtained on appropriate stimulation of various portions of the frontal eye field and of the occipital (17–18) and preoccipital (19) eye fields.

to the most posterior portions of each fissure, are so generally accepted as to require no documentation here. Bilateral destruction of area 17 produces blindness. In the macaque (fig. 6 A), and probably in man, from the inferior part of each calcarine area discharge is made to the adjoining visual association area, the parastriate portion of the occipital region (area 18), and, directly or after relay in this area, to the upper part of the preoccipital eye field (area 19). From

the various portions of these preoccipital and occipital areas impulses are projected to the brainstem to set up following movements of the eyes in the direction of the visual stimulus. Such deviations can be produced experimentally (fig. 5). Walker and Weaver ('40) found that stimulation of the lower part of the occipital eye field in the macaque elicited a deviation of the eyes upward and toward the other side. In our own laboratory (Crosby and Henderson, '48) stimulation of the upper part of this field in the macaque evoked a deviation downward and to the contralateral side. Appropriate midportions of the occipital area are believed to give rotation of the eyes away from the side of stimulation. Excitation of various parts of the preoccipital field (area 19) resulted in the following conjugate eye movements (see pattern on fig. 5): (1) upward; (2) upward and toward the other side; (3) toward the other side; (4) downward toward the other side; and (5) downward. Foerster ('31) showed that excitation of midportions of the human area 19 produces a deviation of the eyes away from the side stimulated.

Fig. 6 A   A diagram of the left cerebral hemisphere of the macaque brain showing the discharge paths from the frontal eye field by way of the cortico-bulbar system and its aberrant cortico-bulbar component and from the occipital (17–18) and the preoccipital (19) eye fields by the cortico-tegmental tract (with at least partial synapse in course) to the contralateral abducens nucleus. The broken lines representing the medial longitudinal fasciculus indicate that the component drawn ascends from the parabducens nucleus on the side opposite the origin of the diagrammed cortico-bulbar system. It terminates in relation with oculomotor neurons which distribute through the oculomotor nerve to the medial rectus muscle on the side of origin of the indicated cortico-bulbar tract. Also diagrammed is the internal cortico-tectal tract, with components from the upper part of the preoccipital (19) and the lower part of the occipital (17–18) eye fields to the rostromedial part of the superior colliculus (S.C.) and from a more ventral part of the preoccipital (19) and the upper part of the occipital (17–18) to the caudolateral part of the superior colliculus.

ABERRANT CORT.-BULB. TR., aberrant cortico-bulbar tract; CORT.-BULB. TR., cortico-bulbar tract; CORT.-TEG. TR., cortico-tegmental tract; INTERNAL CORT.-TEG. TR., internal cortico-tegmental tract; M.L.F., medial longitudinal fasciculus (on right); P. NUC., parabducens nucleus; S.C., superior colliculus; III N., left oculomotor nerve; VI N., left abducens nerve; III NUC., left abducens nucleus.

Fig. 6 A'   A diagram showing the projection of the visual fields on the superior colliculus of the macaque.

From the upper part of the preoccipital eye field (area 19) and the lower part of the occipital field (areas 18 and 17 in the macaque) — that is, from the regions giving upward deviation of the eyes on stimulation — internal cortico-tectal fibers (Crosby and Henderson, '48) discharge to the rostral and

FRONTAL EYE FIELD

19
18
17
18
17
19
S. C.
III NUC. M.L.F.
P. NUC.
CORT.-BULB. TR.
INTERNAL CORT.-TEG. TR.
III N.
VI NUC.
ABERRANT CORT.-BULB. TR.
(IN MEDIAL LEMNISCUS)
CORT.-TEG. TR.
VI N.

A

SUPERIOR COLLICULI

PINEAL BODY
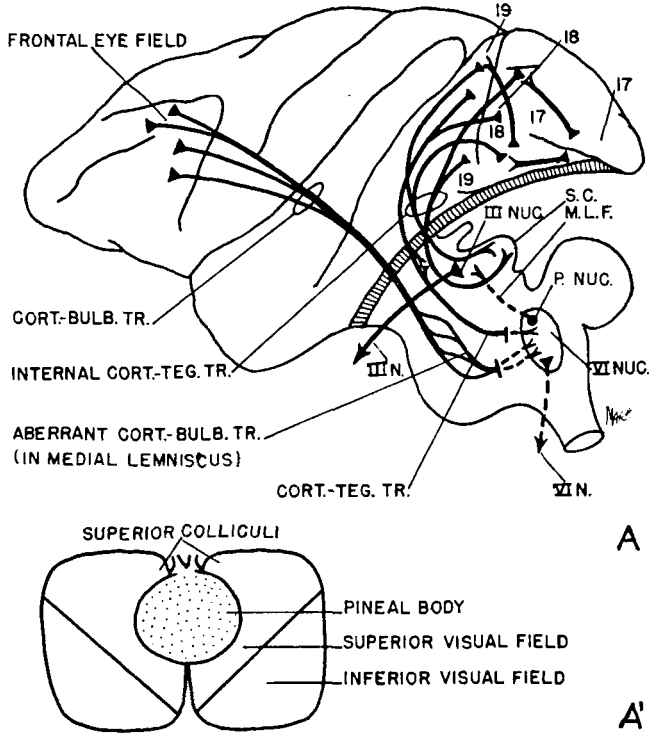SUPERIOR VISUAL FIELD
INFERIOR VISUAL FIELD

A'

Figure 6 A

medial portions of the superior colliculi (fig. 6 A). The more ventral part of the preoccipital areas and the upper part of the occipital areas furthering downward deviation of the eyes project functionally similar cortico-tectal fibers to the lateral and caudal parts of the collicular regions (fig. 6 A). These relations for area 19 have been documented by the work of Peterson and Henneman ('48). Such cortico-tectal

paths end in relation with the primitive localization pattern impressed upon the superior colliculi by the terminations of the optic tract fibers. Both types of impulses are discharged to the oculomotor nuclei and, through them, to the trochlear nuclei to give appropriate upward or downward turning of the eyes. Indeed it would seem probable that the localization patterns in the preoccipital and occipital areas are projected back upon them — and, in this sense, determined — by the phylogenetically earlier established pattern for eye deviations found in the superior collicular regions, and in the connections of these collicular areas with specific portions of the oculo-motor nuclei.

The internal cortico-tectal tract has been described by various observers under a variety of names. Thus it is the "Rinden-Sehhügelfasern" of Probst ('02, cat), the cortico-fugal fibers of Barris, Ingram and Ranson ('35, cat), the pallio-tectal tract of Beevor and Horsley ('02, various mammals), or the cortico-mesencephalic tract of Beevor and Horsley ('02) and Mettler ('35b, monkey), and the internal cortico-tectal system of Huber and Crosby ('43). It was subdivided into an occipital division (consisting of fascicles from the occipital lobe) and a preoccipital division (constituted by fibers from preoccipital areas) by Crosby and Henderson ('48) and by Lemmen ('51).

Possibly the portions of the occipital and preoccipital eye fields concerned with horizontal deviations of the eyes discharge also to the superior colliculi, their impulses serving to inhibit the reflex discharge of this region which results in conjugate horizontal deviation of the eyes. Since horizontal deviations are thought to be dominant in higher mammals such an inhibitory discharge would further vertical eye movements. Certainly the major descending paths (the cortico-tegmental tracts) from the horizontal portions of the pre-occipital and occipital areas by-pass the superior colliculi in the macaque and most probably in the human brain. Each cortico-tegmental system continues downward in the macaque

brain, through the tegmental area of the midbrain to end, primarily, in the contralateral abducens nucleus, where it sets off the usual arcs producing contraction of the homolateral lateral rectus and the contralateral medial rectus muscle. The cortico-tegmental system may also discharge to the vestibular centers (lateral and medial vestibular nuclei) of both sides since Spiegel ('33) found that in the cat he was unable to elicit following movements of the eyes in the horizontal direction from stimulation of the appropriate portion of the occipital cortex after bilateral destruction of the vestibular areas. From these areas (fig. 2) discharge is made through the medial longitudinal fasciculus for horizontal conjugate deviation of the eyes (see p. 440). Anatomical evidence is lacking for such cortico-vestibular connections.

Cases of pinealoma indicate that relations similar to those in the macaque exist in man (Crosby, '50). As the pineal body enlarges it presses directly upon the superior colliculi (fig. 6 A'), beginning at their rostral poles, and so interferes with the functioning of the cortico-tectal pathways from the upper parts of the preoccipital and the lower part of the occipital eye fields, stimulation of which fiber systems produces an upward deviation of the eyes. Consequently the existence of a pinealoma is often indicated early, not only by increased intracranial pressure and possible loss of light reflexes, but also by an interference with following movements in the upward direction, although the patient may be able to look up voluntarily or may show no abnormalities of eye movement when tested for vestibular reflexes. Later, a loss of downward following movements, or oculomotor palsies, may occasionally supervene. In any case, the patient retains his ability to follow a finger moving in the horizontal plane, evidence that the pathways for horizontal following movements do not have a necessary synapse in the superior colliculi. Cases illustrating the above statements are numerous in clinical literature.

An experimental study of certain ablations in the preoccipital and the occipital areas in monkeys (Henderson and

Crosby, '52) yielded some interesting results in relation to following movements and optokinetic responses. A macaque was immobilized in a stereotaxic apparatus so that the head could not be moved. The room was dimly lighted and the inside of a box in which the monkey was placed was painted a dull black to absorb excess light rays. At one end of the box were three openings. The center opening contained a drum which could be rotated in either direction and which had alternating black and white vertical stripes about a centimeter wide. On either side of the drum was a small window covered over by special glass which permitted the observer to watch the monkey although the monkey could not see the observer. Behind the monkey was a light which was focused on the revolving drum. If the monkey's attention was on the drum, his eyes followed the stripes in the direction of its slow, steady rotation and then quickly came back to center. As the rotation was continued these following movements became a rhythmic optokinetic nystagmus with a slow component in the direction of the rotation of the drum and a quick component to the other side. If the drum was rotated in the opposite direction the components of the nystagmus were reversed. In cases of suspected lesions in occipital and preoccipital regions of the human cortex, similar tests are often carried out. Droogleever Fortuyn and van der Waals ('40) used a rotating drum, large enough so that the patient could be placed inside of it. Otherwise a somewhat larger optokinetic drum of the type described for experiments on the monkeys is used. The presence of a nystagmus, with the slow and quick components in the expected directions, indicates that areas 18 and 19 are intact. Thus, perfectly normal individuals under proper conditions exhibit an optokinetic nystagmus. The individual watching the telegraph poles from a steadily moving train shows a slow deviation of the eyes in the direction of the poles and a quick return (Walsh, '47). This nystagmus has been called railroad nystagmus (Bárány, '21). A person sitting perfectly quiet but with his attention

fixed on a succession of moving objects likewise may show optokinetic responses.

After a group of monkeys had been tested for normal optokinetic responses in the horizontal plane, destructive lesions were made in various portions of the preoccipital and occipital areas (Henderson and Crosby, '52). With bilateral ablation of those parts of the preoccipital (area 19) and the occipital (area 18, in this case) areas related to deviation of the eyes in the horizontal plane, optokinetic responses toward either side were abolished; a unilateral destruction of the same regions resulted in a loss of following movements away from the side of the ablation. If only the part of the preoccipital field concerned with conjugate horizontal deviation of the eyes was involved in a lesion, the intact ipsilateral occipital area may still permit a normal turning of the eyes (or a normal optokinetic response) toward the other side. Lesions in comparable areas of the human cortex are indicated also by interference with optokinetic responses. Stimulation or irritative lesions in the appropriate portions of the preoccipital and/or occipital regions may produce a nystagmus of optokinetic type in either monkey or man, with the quick component occurring toward the side of the irritation. After bilateral destruction of those portions of the frontal areas of the macaque cortex related to voluntary eye deviations, tests with the optokinetic drum showed an increase in the optokinetic responses in the horizontal plane. Each frontal eye field may suppress the activity of both preoccipital eye fields, consequently a lesion involving the horizontal region of one frontal eye field does not change the optokinetic response. However, if the lesion is restricted to the lower half of one frontal eye field, following a homolateral preoccipital lesion, the optokinetic response when the drum is rotated toward the side of the lesion is reduced.

Optokinetic responses have been studied by many clinicians (as for example, Cogan and Loeb, '49). Such responses presuppose that the patient has some ability to see (Walsh, '47, and others), although an uninjured macula is not essential

to such responses according to many observers (Fox and Holmes, '26; Dodge and Fox, '28; Walsh, '47; and others). Bárány ('21), on the basis of tests of two individuals having hemianopsia, decided that optokinetic responses are normal when the drum is rotated away from the side but absent when it is rotated toward the side of the hemianopsia. Ohm ('32; see also Cords, '26; Strauss, '33; Walsh, '47) showed that the loss of optokinetic responses exhibited by Bárány's patients depended upon a destruction of the efferent paths (internal cortico-tectal tracts) from the occipital and pre-occipital regions along with that of the visual radiations responsible for the hemianopsia.

Stenvers ('24) and Fox and Holmes ('26) considered that the discharge paths from the occipital eye fields relay in the frontal cortex on their way to lower centers, a point of view to which Cords ('26), Strauss ('33), Crosby and Henderson ('48), Henderson and Crosby ('52), and others have been opposed. Blocking of optokinetic responses in subprimates (cats and dogs) by lesions at superior collicular levels has been described by Scala and Spiegel ('38).

The question as to whether or not optokinetic responses can be inhibited voluntarily and, if so, under what conditions and in what forms, has been of considerable interest to clinicians and experimentalists alike. According to Cogan and Loeb ('49) such optokinetic responses cannot be inhibited voluntarily in man. However, various opthalmologists have found that such responses may be prevented if the individual will look through or beyond the revolving optokinetic drum (Walsh, '47; Kestenbaum, '46). Such an inhibition appears to be difficult or even impossible to maintain for a great length of time, presumably because of the strain on the eyes and the difficulty in fixing the attention. The monkeys tested by Henderson and Crosby ('52), probably because of their intense curiosity and fear, were able to inhibit optokinetic responses for a considerable time, even when they were looking directly toward (though probably through) the drum. Certainly under ordinary, rather than experimental, conditions

all normal individuals frequently refrain from permitting their eyes to follow moving objects in order to fix them upon those objects in which they are interested. Only as attention to the outside world lags do the eyes follow idly anything (or any person) moving slowly and steadily back and forth (or up and down) across the field of gaze.

VOLUNTARY DEVIATIONS OF THE EYES
IN THE HORIZONTAL PLANE

Voluntary movements of the eyes differ from following movements in that they represent the ability to shift the eyes at will from one object to another quite unconnected with the first. Such voluntary eye deviations depend upon intact frontal eye fields and uninjured connections from these cortical centers to the eye muscle nuclei. They are often associated with head and sometimes with body movements.

In 1874 Ferrier described eye deviations in the horizontal plane from electrical stimulation of a region in the frontal lobe of the monkey, rostral to the arm area of the motor cortex. Since this early work of Ferrier, eye deviations have been demonstrated by various methods in the frontal lobes of carnivores (Risien Russell, 1895; Spiegel and Scala, '36; Smith, '40, '49), of monkeys (Ferrier and Yeo, 1884; Horsley and Schafer, 1888; Beevor and Horsley, 1888, 1890; Mott and Schafer, 1890; Sherrington, 1893; Risien Russell, 1894; Jolly and Simpson, '07; Vogt and Vogt, '07, '19; Levinsohn, '09; Smith, '40, '49; Crosby, Yoss and Henderson '52; and others), of the gibbon (Fulton, '32; and Hooker, Humphrey, Chambers and Crosby, to be published), of various apes (Grünbaum and Sherrington, '01; Leyton and Sherrington, '17), and of man (Foerster, '31, '36; Penfield and Boldrey, '37; Penfield and Erickson, '41; Spiegel and Sommer, '44; Rasmussen and Penfield, '48; Penfield and Rasmussen, '50; and others). All of these observers obtained conjugate deviation of the eyes toward the side opposite stimulation; sometimes the eyes had a slight upward or downward tilt. Some of these workers demonstrated eye movements in other planes (notably Beevor

and Horsley, 1890; Risien Russell, 1894; Mott and Schaefer, 1890; Smith, '36, '49; and Penfield and Rasmussen, '50). Convergence (Risien Russell, 1894), pupillary changes (Vogt and Vogt, '07, '19; Spiegel and Sommer, '44; Smith, '49), and nystagmus (Smith, '49; Crosby, Yoss and Henderson, '52; and others) have also been described.

In recent years a group at Michigan (Crosby, Yoss and Henderson, '52) have interested themselves in laying out the pattern of eye movements on the frontal lobe in the macaque. It was easy to obtain horizontal deviation of the eyes to the opposite side. Changes in the strength and the frequency of the stimulus and in the depth and the kind of anesthesia indicated that the horizontal movements were only a part of the pattern for eye movement. This pattern extends over the lateral surface of the frontal lobe from near the superior sagittal sinus ventralward, along the front border of the arcuate fissure, to a region dorsal to the lateral fissure. It is not our purpose to discuss here the cytoarchitectural fields corresponding to the frontal eye field as here laid down from experimental studies of eye deviations in the macaque. This frontal field of the macaque falls within FD of Bonin and Bailey ('47), the eye movements listed in the succeeding paragraph under numbers 5 to 7 apparently having been elicited from their FD T. Those observers interested in making a comparison between the cytoarchitectural and the experimental maps are referred to the figures, the texts and the bibliographies in the contributions of Bonin and Bailey ('47, macaque), Bonin ('49 and '50, primates), and Bailey and Bonin ('51, man) and figure 5 of the present paper.

The pattern of eye deviations obtained by Crosby, Yoss and Henderson ('52) is indicated in figure 5, p. 455, and is as follows from above downward: (1) conjugate deviation of the eyes downward and toward the other side; (2) divergence; (3) conjugate horizontal deviation of the eyes toward the other side; (4) conjugate deviation of the eyes upward toward the other side; (5) conjugate horizontal deviation of the eyes; (6) divergence; (7) conjugate deviation of the eyes downward

and toward the opposite side. The dorsoventral extent of this area related to eye movements is roughly divisible into two portions by the so-called principal fissure. The portion allocated to deviation of the eyes upward and toward the other side lies at the caudal tip of this fissure. The pattern below the fissure is a mirror-image of that above it, so that, in each frontal eye field, there are two areas, stimulation of which produces conjugate horizontal deviation of the eyes toward the opposite side; two regions from which divergence can be elicited; and two which are related to conjugate deviation of the eyes downward and toward the other side. The region for deviation upward and toward the other side is also doubled. Accompanying these other movements were some pupillary changes, but these are difficult to assess in view of the variations in the depth of anesthesia and they have not been reported.

This mirror-image duplication of pattern (fig. 5) suggests that one of these patterns for eye deviation may be the major area for voluntary conjugate deviation of the eyes in various directions; the other constitutes a second (Sugar, Chusid and French, '48; and others) or supplementary (Penfield and Welch, '51; Penfield and Rasmussen, '50) motor area comparable in general to such second or supplementary motor areas described in relation to the motor cortex by a number of observers (Garol, '42, cat; Sugar, Chusid and French, '48, cat; Penfield and Rasmussen, '50, man; Lauer, '52, macaque; Woolsey et al., '52, chimpanzee; and various other workers). This matter is reserved for further discussion when some of the experiments now under way on the interrelations of the frontal eye fields with other cortical centers shall have been completed.

Bilateral stimulation of portions of the frontal eye fields in the macaque have also been carried out (Risien Russell, 1894; Crosby, Yoss and Henderson, '52). Simultaneous bilateral stimulation of the portions of these fields immediately caudal to the principal fissure, which are concerned with deviations of the eyes upward and toward the other side,

evoked a conjugate upward deviation of both eyes. Bilateral excitation of the regions above the principal fissure related, on unilateral excitation, to conjugate horizontal deviation of the eyes toward the other side, gave an "eyes front" position. Obviously, then, gaze directly upward, or directly forward and, probably, directly downward depends upon the coopera-tive action of the corresponding parts of both frontal eye fields. Destruction of one horizontal area may produce a turn-ing of the eyes toward the side of the lesion (although this condition is very transient in the monkey). Moreover, the animal is unable to turn his eyes voluntarily toward the side opposite the lesion, although he will still show following and reflex eye movements. This paralysis of voluntary movement is also not permanent, although it persists longer than the forced deviation.

In human cases where the frontal portion of the brain had been exposed for operative procedures, Foerster ('31, '36) stimulated the posterior end of the middle frontal gyrus and elicited horizontal deviation of the eyes. Others have docu-mented this deviation in man, notably Penfield and Boldrey ('37); Penfield and Erickson ('41); Rasmussen and Penfield ('48); and Penfield and Rasmussen ('50), who evoked eye movements in various directions from the frontal eye fields including deviations downward or upward toward the other side. Their results are in general agreement with those ob-tained in the experimental studies of the frontal eye fields in the macaque (Crosby, Yoss and Henderson, '52) and the gib-bon (Hooker, Humphrey, Chambers and Crosby, to be pub-lished) although no definite pattern arrangement of these eye movements has been indicated by Penfield and his asso-ciates.

The frontal eye fields are connected by cortico-bulbar com-ponents of the pyramidal system with the appropriate eye muscle nuclei. As early as 1868 Prevost reported a deviation of the head and eyes associated with hemiplegias from internal capsule lesions in man. Dejerine ('14), in his studies of the human aberrant pyramidal system, showed an aberrant path-

way to the abducens nucleus. Various experimental studies
of the cortico-bulbar component of the pyramidal system re-
lated to voluntary deviation of the eyes in the horizontal plane
have been carried out. Hirasawa and Katô ('35) and Levin
('36), following ablations of portions of the frontal eye field
in the macaque, traced degenerated fibers to the midbrain
tegmentum; Mettler ('35a), after destruction of the frontal
lobes in such monkeys, demonstrated degenerated fibers to
"eye-motor" nuclei. In 1923 Bárány, Vogt and Vogt (maca-
que) had reported a series of experiments showing the rela-
tions of the frontal eye fields to the vestibular areas. Their
results and those of Spiegel and Scala ('36, cat; see also
Spiegel and Sommer, '44) suggest that connections for volun-
tary conjugate horizontal deviation of the eyes may be made
from the frontal eye fields through the vestibular centers.
After bilateral injury of the vestibular nuclei in cats, Spiegel
('33) was unable to produce horizontal deviation of the eyes
from cortical excitation. Undoubtedly, then, cortico-vesti-
bular connections do exist although the precise origin and
course of the tract or tracts in this arc are still to be estab-
lished. However, in the presence of an abducens component
of the cortico-bulbar system discharging from the horizontal
portions of the frontal eye field of one side to the abducens
nucleus of the other side, it seems probable that the role of the
cortico-vestibular systems may be to supplement the functions
of the cortico-bulbar tract. They affect the voluntary devia-
tion either by inhibiting the vestibular reflex arcs through the
contralateral medial and lateral vestibular nuclei (fig. 2)
which tend to rotate the eyes away from the direction of the
voluntary (and following) responses or by facilitating the
homolateral vestibular reflex arcs, which function in horizontal
deviation of the eyes in the directions of the voluntary re-
sponse or by serving both inhibitory and facilitatory functions
with the view of furthering the appropriate response.

In some of the monkeys at Michigan (Crosby, Yoss and
Henderson, '52), lesions were placed in the horizontal area
of one frontal eye field. In the more favorably stained ma-

terial prepared by Marchi technique from these operated brains, cortico-bulbar fibers (fig. 6 A) can be traced from the horizontal part of one frontal eye field through the genu of the internal capsule into the base of the midbrain. Beginning at oculomotor levels, fascicles separate off — a few at a time — to enter the overlying medial lemniscus as an aberrant pyramidal system. They are joined, at lower pons levels, by a few fibers directly from the pyramidal system. The combined bundles cross the midline to end in the contralateral abducens nucleus. From this nucleus relay is made to the ipsilateral lateral rectus muscle and, through the medial longitudinal fasciculus, to the oculomotor nucleus for innervation of the contralateral medial rectus muscle, thus providing for conjugate deviation of the eyes away from the side of origin of the related cortico-bulbar system. Thus the frontal eye fields, like areas 18 and 19 and the vestibular nuclei, project upon the pre-established reflex pattern related to the conjugate horizontal deviations of the eyes. Therefore, destruction of these fasciculi blocks such horizontal deviations, whether one is dealing with reflex, automatic, or voluntary responses. Data from clinical cases indicate that this pattern arrangement is substantially the same for man as for the macaque (see Crosby, Yoss and Henderson, '52).

RELATIONS OF FRONTAL EYE FIELDS TO RECIPROCAL INNERVATION OF EYE MUSCLES

In 1893 Sherrington demonstrated that if the lateral rectus of one eye and the medial rectus of the other are cut in the monkey, so that the eyes are deviated away from the side of the destroyed lateral rectus, stimulation of the appropriate portions of the frontal eye field may still bring the eyes back to the midplane. He considered that deviation of the eyes is a resultant of the interaction of the muscles on the two sides of the eyeball — that is, as the lateral rectus muscle contracts, the medial rectus correspondingly relaxes. Stimulation (Crosby and Yoss, to be published) of the horizontal portions of the left frontal eye field above the principal fissure follow-

ing section of the right lateral rectus and the left medial rectus muscles did not produce such a return of the eyes to the midplane in the macaques. However, stimulation of the corresponding region below the principal fissure did give the return to the midline indicated in Sherrington's experiments. Their results indicate a functional difference between the two horizontal portions of the frontal eye field.

INTRACORTICAL ASSOCIATIONS FUNCTIONING IN EYE DEVIATION

Naturally, there are important interrelations between the frontal and the occipital and preoccipital eye fields, the evidence for which is far from complete. Some facts, however, are suggestive of the richness and the significance of these intracortical associations.

Of course, voluntary eye movements are initiated not only by the things one sees but by those one hears, by the objects that one touches, and by merely the memory of some past experience — by the thousand and one incidences of daily life. The connections to the frontal cortex from various association areas of the cerebral cortex are numerous and of widely different import. It seems very probable that either directly and/or after secondary synapse the frontal eye fields are stimulated by impulses reaching the frontal regions of the hemisphere over such association paths, although the evidence for this needs further documentation. However, an example of this type of connection may be used to illustrate such relations. It was stressed earlier that the impulses projected on the visual cortex (area 17) of one side are from the contralateral visual field and that the usual response to such impulses is a horizontal deviation of the eyes toward that field. From area 17 (fig. 6 A) discharge is made to homolateral area 18, and from area 18 to contralateral area 18 and homolateral and contralateral areas 19 (McCulloch, '48, '49, macaque). From the occipital region (area 19) impulses of a suppressor type are relayed forward to the homolateral and contralateral area 8, as well as to various other cortical areas. The richness

of the cortical interrelations in primates as revealed by neuronography has been well presented by Bonin, Garol and McCulloch ('42), McCulloch ('49), and Bailey and Bonin ('51). Some of the impulses discharged forward from the occipital to the frontal lobe and which reach the frontal eye fields directly (and also after synapse) appear to be facilitatory. Clark and Lashley ('47) showed that lesions involving the frontal eye field, or the superior longitudinal fasciculus between the occipital and the frontal areas, interfere with horizontal deviation of the eyes in response to visual stimuli from the lateral part of the contralateral visual field — that is, produce their so-called homonymous hemianopsia. An alteration in the response to visual stimuli — but not a true hemianopsia — was obtained by Kennard ('39; see also Kennard and Ectors, '38) following ablations of portions of the frontal lobe in monkeys. This condition represents actually a false or pseudohemianopsia. In such a pseudohemianopsia there is no damage to the visual pathways or visual cortex, no blindness, no interference with visual reflexes or following movements or fixation of the eyes. However, there is no way to translate the visual impulses into voluntary responses because either the association pathways or the frontal eye field, which are essential parts of the neuron arcs underlying these responses, are destroyed. Consequently conjugate horizontal deviation of the eyes toward an object in the lateral visual field does not occur as a voluntary movement.

There are direct connections from the horizontal area of the frontal eye field to areas 18 of the same and of the opposite side and to adjoining portions of area 19 directly and, at least homolaterally, after relay in area 18. There is reason to think that fiber bundles carry facilitatory impulses to homolateral and contralateral area 18 and inhibitory impulses to homolateral and contralateral area 19, and that area 18 connects with and fires homolateral area 19 (Crosby and Henderson, '48; McCulloch, '49; and elsewhere). However, the anatomical details of these connections are yet to be revealed. Evidence now at hand suggests that destruction of the horizontal por-

tion of the frontal eye field below the principal fissure in the macaque releases the activity of the contralateral occipital and preoccipital areas, as indicated by an increase in optokinetic responses when the drum is rotated toward the side of the lesion. Destruction of the horizontal field above the principal fissure either does not affect the optokinetic discharges or possibly increases them slightly toward both sides (Crosby and Yoss, to be published). Finally, destruction of both horizontal fields on one side does not appear to affect optokinetic discharges toward either side (Henderson and Crosby, '52).

Risien Russell (1895) showed that if the frontal eye field of one side and the occipital eye field (area 18) of the other are stimulated independently, with stimuli adequate to set up from each typical responses (which would be in opposite directions with respect to each other) and then the two areas are stimulated simultaneously, that the eyes turn in the direction determined by the frontal eye field. When bilateral destruction of the horizontal portion of the frontal eye field was carried out in our laboratory (Henderson and Crosby, '52), the optokinetic responses obtainable on activation of areas 18 and 19 were greatly increased, since apparently the animal could no longer inhibit them voluntarily. As already noted (see p. 462), such voluntary inhibition can be exerted by a person with an uninjured brain if he will look through or to the side of an optokinetic drum rather than watch the stripes (Kestenbaum, '46; Walsh, '47). The macaque shows a like voluntary inhibition when his attention is centered elsewhere than on the drum.

After destruction of the preoccipital and occipital fields, stimulation of the part of the horizontal area of the frontal eye field above the principal fissure still produces normal conjugate deviation of the eyes toward the opposite side. Under similar conditions excitation of the lower half of the horizontal area, that is the part below the principal fissure, usually yields no response. This suggests a further functional difference between the upper and the lower part of

the horizontal area of the frontal eye field. Obviously, the lower part of the frontal eye field depends, for normal expression, on areas 18 and 19. We are inclined to believe that this is another expression of the inhibitory and the facilitatory relations existing between the frontal and the occipital and preoccipital eye fields and are hoping that further studies may clarify this point. Neuronography studies of McCulloch ('49) have indicated that inhibitory impulses do pass forward from area 18 to area 8, which falls within such frontal fields, although possibly by way of the caudate nucleus (McCulloch, p. 239).

EYE DEVIATIONS FROM MOTOR CORTEX

Finally, deviation of the eyes in various planes, including the horizontal, have been elicited from the human motor cortex in the region near the central fissure by Penfield and Rasmussen ('50) and from the motor area of the macaque by the Michigan group (Crosby, Yoss and Henderson, '52). The former observers considered that such eye deviations — and also those obtainable from the frontal eye fields — are adverse movements of an essentially similar type. Before assessing them, certain facts concerning these eye deviations obtainable from the motor area should be taken into account. In the first place, in the macaque at least, they are much more difficult to elicit on stimulation than are the face and upper extremity movements which can be evoked from the surrounding motor cortex, or than the eye deviations appearing on suitable excitation of the frontal eye field. Furthermore, their destruction is not associated with any obvious interference with voluntary eye deviations such as is evident when the frontal eye field is destroyed. They appear to have more of the character of automatic associated movements of cortical type than of voluntary eye movements. Leyton and Sherrington ('17) obtained them many years ago and regarded them as accompaniments of face and forelimb movements.

In conclusion, it may be pointed out that all levels of the nervous system from cervical cord to frontal cortex may affect so simple a movement as the horizontal deviation of the eyes. The connections and relations here discussed are a very small part of possible interrelations of the various centers concerned with such simple eye movements. One is amazed — and appalled — at the infinite complexity of the nervous system.

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