INTRODUCTION

Bianchi described a neglect of visual stimuli on the side contralateral to a unilateral frontal lobe lesion in monkeys. This was confirmed by Ferrier and Turner and Jacobsen. Kennard and Kennard and Ectors showed that the neglect occurred after unilateral removal of Brodmann’s area 8, which corresponds, though only approximately, to the frontal eye-fields — the region of the frontal lobe where electrical stimulation produces highly reproducible contralateral conjugate eye movements, whose precise direction depends on the locus of stimulation. Other frontal lesions did not cause a neglect. Subsequently, Clark and Lashley, Welch and Stuteville, Denny-Brown and Brucher all found contralateral neglects after unilateral frontal eye-field lesions.

This neglect has always been shown by an absence of response to food or frightening visual stimuli. Kennard’s technique of recording the order in which the monkey picks up a row of peanuts was a more systematic characterization, but she did not control or measure head and eye movements. Since the other main effect of the lesion is ipsilateral deviation of the head and eyes and circling of the body, it is possible that the neglect is an indirect result of the oculomotor disturbance.

All tests, apart from those using a fear response, have used responses that are spatially related to the stimulus. So a second explanation of the neglect is a disturbance of limb movements to the contralateral side. That there is a motor change of some kind is shown by the fact that these monkeys show a very strong preference for their ipsilateral hand, but whether the visual neglect causes the change in motor behaviour or vice versa, or whether both are a product of something else, is unclear.
The neglect has other properties that have been consistently reported but are not easily interpreted. It is always transient, with complete recovery occurring within a few weeks, but there is no evidence which distinguishes loss of the impairment from behavioural compensation for an enduring disorder. Subsequent removal of the contralateral eye-field results in a deficit that, apart from laterality, is indistinguishable from the original. Yet simultaneous removal of both eye-fields has generally been reported as having either no effect on responsiveness to visual stimuli, or as producing at the most a slight 'inattentiveness'. This discrepancy between the effects of unilateral and bilateral lesions has been a major difficulty in formulating an explanation of the visual neglect.

The present study was designed to analyse this neglect further by mapping visual fields before and after frontal eye-field lesions, using a perimeter specially designed for use with monkeys. It provides quantitative data on the magnitude and time course of the neglect, and by controlling for eye and head movements and having the stimulus and response spatially independent, it tests directly the two hypotheses outlined above concerning the origin of the neglect.

**METHOD**

*The perimeter*

The apparatus and technique used have already been described in detail elsewhere. The perimeter consisted of a square matrix of 120 stimulus bulbs mounted at 5° intervals over the inside of part of a spherical shell of radius 50 cm. At the centre of the matrix was a 2° square plane mirror mounted so that a monkey looking through a 2 cm peep-hole at the centre of curvature of the shell saw a reflection of his own eye. The stimulus bulbs subtended 1° had a normal luminance of 5,500 cd/sq.m, which could be dimmed to 550 cd/sq.m, against a background of 0.34–0.85 cd/sq.m, and provided a test flash of 50 msec. A 16 mm cine camera mounted behind the fixation mirror was used to photograph the monkey's eye. Four 17,000 cd/sq.m floodlights, mounted round the perimeter shell and aimed at the peep-hole, provided both light for photography and corneal reflexions for determining the monkey's direction of gaze (see below). At the top of the shell there was an electromagnetic buzzer that could generate a 50 msec click.

The front wall of the animal's compartment contained the peep-hole, which was surrounded by adjustable metal shields, arranged so that when the monkey pressed his head into the mask his right eye was against the peep-hole. Below the face mask was a foodwell into which CIBA banana flake pellets could be delivered automatically. The two retractable response levers were 8 cm below the foodwell and 38 cm apart, conveniently adjacent to the animal's left and right hands.

*Training and testing*

Using customary operant shaping techniques the monkeys were taught to press their right eye against the peep-hole and fixate the mirror. When the monkey's eye was in position, the experimenter initiated a trial by operating the stimulus generator.
and the camera shutter, which were synchronised, and moving the response levers into the testing box. Apart from this, control of the experiment was entirely automatic. There were two kinds of trial. On one, the stimulus was a 50 msec click (N) and if the monkey pressed the right lever (R\text{N}) within 6 sec a food pellet was delivered to the food-cup, which was illuminated for 2 sec. But if he pressed the left lever (L\text{N}) there was no reward and the house light went out for 5 sec. On the other kind of trial, there was a 50 msec test flash from one of the stimulus bulbs coincident with the click (SN). In this case the monkey was rewarded for pressing the left lever (L\text{SN}) and the house light went out if he pressed the right lever (R\text{SN}). If the monkey failed to respond within 6 sec of the stimulus presentation, the trial was ended and the response levers withdrawn. Monkeys normally responded within the first 1–2 sec after stimulus presentation, and complete failure to respond was very rare. Up to 300 trials were given in each testing session. The two kinds of trial and the position of the test flash on SN trials were selected in a pre-determined random order which was changed frequently.

To provide a comparison with earlier studies, we also looked at the monkeys' accuracy of food retrieval, hand preference, and general behaviour in their home cages.

The perimetric technique

The direction of gaze on a particular trial was found by comparing the eye photograph for that trial with a set of 49 standard reference photographs for which the direction of gaze was known. To prepare the standard photographs, the central mirror was removed, a moveable fixation mirror was plugged into one of the bulb sockets, and 20 trials were run. When the 20 photographs from these trials were compared, it was found that all or most of them showed the same direction of gaze, presumably aimed at the fixation mirror. One of these was then used as the standard for that fixation position. This was repeated for a square matrix of 49 positions at 5° intervals, extending from 5° above the fixation mirror to 25° below and to 15° on either side. The final array of standard eye photographs is reproduced in Weiskrantz and Cowey\textsuperscript{45}. This did not cover the entire stimulus array because during training fixations were very rarely observed outside these 49 positions. It was originally intended that each monkey should have his own set of standard eye photographs, as in the previous studies\textsuperscript{13,14}, but after comparing their eye photographs with the set made for monkey P6 it was found that there was no discernible difference between the eye photographs of different monkeys fixating the same point. To determine the direction of gaze on a particular trial, the eye photograph for that trial was projected onto the array of standards which was moved round until, when the 4 corneal reflexions of the projected image were superimposed on those of the standard, the pupils of the two photographs were concentric — the pupil diameter obviously varied considerably from trial to trial. This process of matching the projected image with one of the standards was made easier by their having opposite figure-ground relationships, for the prints of the standard photographs were positive and the projected images were negative. With practice it became easy to compare two superimposed

*Brain Research, 30 (1971) 1–24*
images in this way and the technique could be used to determine the direction of gaze to a greater accuracy than used here. Since fixation was referred to the nearest point in a square matrix of points arranged 5° apart horizontally and vertically, the greatest error is half the angular distance between two points on a diagonal, *i.e.* about 3.5°. Errors caused by the small changes in head position that were possible in the perimeter and by torsional movements of the eyeball have been analysed in detail elsewhere\[^{14,16}\], and are always less than 5°. Eye movements or withdrawal of the head from the peep-hole during the presentation of the stimulus showed clearly on the eye photographs and these trials were discarded. Apart from the immediate post-operative period (see below), fewer than 1% of trials had to be discarded in this way.

The monkeys were tested 5 or 6 days a week and data from over 80,000 trials were collected. Because the analysis was so time-consuming only a fraction of these trials could be analysed in detail. This loss was unavoidable since neither the nature nor the time course of the possible effects were known in advance. Blocks of 500 consecutive trials were analysed, giving two presentations of each stimulus bulb, and a visual field plotted. Testing was re-started on the day following the operation, and the first 500 trials were selected as soon as the monkey performed 50 trials or more in a single session with his eye in position against the peep-hole. Subsequent blocks of trials were selected for analysis at intervals which varied according to the animal’s rate of recovery (see below).

Because of the complexity of the behaviour involved, an impairment in the perimeter could be caused by any one of a number of changes other than a field defect. For example, a monkey that perseverated on the right response lever would appear to have a total field defect. We attempted to distinguish and control for impairments other than field defects in several ways:

1. By using unilateral lesions the ipsilateral half-field was used as a control for the contralateral half-field.

2. By analysing the false positive errors (L\(N\)) as well as the false negatives (R\(SN\)), looking particularly at the way in which the distribution of errors changed between pre- and post-operative testing.

3. By varying the stimulus intensity and analysing the changes in error scores, it was possible to show the extent to which a possible defect was stimulus-bound.

4. By changing the fixation point and replotting the visual field, it was possible to show whether an impairment was related to the retinal position of the stimulus or to its position with respect to the apparatus and the monkey’s head and body. Each monkey was tested with the fixation mirror 15° to the right of the centre of the perimeter and with it 15° to the left.

In looking at the effect of using a dimmer stimulus or changing the fixation point, a balanced experimental design was always used:

- 250 trials with condition A (*e.g.* normal stimulus)
- 250 trials with condition B (*e.g.* dim stimulus)
- 250 trials with condition B
- 250 trials with condition A

*Brain Research, 30 (1971) 1–24*
FIELD DEFECTS AND FRONTAL EYE-FIELDS

TABLE I

LESIONS MADE ON THE PERIMETER SUBJECTS

The numbers in brackets give the date of the operation in months from the start of training.

<table>
<thead>
<tr>
<th>Monkey</th>
<th>Lesion</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>Killed</th>
</tr>
</thead>
<tbody>
<tr>
<td>P2</td>
<td>Left principalis (23)</td>
<td>Right frontal eye-field (24)</td>
<td>—</td>
<td>—</td>
<td>(29)</td>
<td></td>
</tr>
<tr>
<td>P3</td>
<td>Right frontal eye-field (12)</td>
<td>Left frontal eye-field (15)</td>
<td>Right superior colliculus (23)</td>
<td>Left superior colliculus (28)</td>
<td>(29)</td>
<td></td>
</tr>
<tr>
<td>P4</td>
<td>Bilateral frontal eye-field (17)</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>(22)</td>
<td></td>
</tr>
<tr>
<td>P6</td>
<td>Left frontal eye-field (12)</td>
<td>Right frontal eye-field (19)</td>
<td>—</td>
<td>—</td>
<td>(23)</td>
<td></td>
</tr>
</tbody>
</table>

Using the data from all 1,000 trials, the visual fields for each condition were then drawn and compared.

The effect of frontal eye-field lesions on accuracy of fixation in the perimeter was also investigated. These results are presented and discussed in a separate paper.

Subjects and surgery

Four immature male rhesus (Macaca mulatta), 1–2 years old and weighing 2–3 kg were used. All were experimentally naive at the start of training, and except for simple neurological tests after operation, they were not tested on anything except perimetry. All operations were performed with sterile techniques, using deep Nembutal anaesthesia.

Except for P4 they were given serial unilateral lesions, being retested between operations until their performance had either returned to normal or stabilised. The lesions made are shown in Table I.

The unilateral frontal eye-field lesion was the primary lesion being studied and five of these were made. P4 was given a bilateral frontal eye-field lesion. An impairment in the perimeter after a bilateral lesion is difficult to interpret because of the absence of a control half-field, but if P4 had shown no impairment this would have been of considerable interest. P2 was initially given a small lesion in the region of the left sulcus principalis, anterior to the frontal eye-field, to control for effects that might be produced by any small unilateral frontal lesion. Since monkeys with infero-temporal, striate, or retinal lesions had already been tested in the perimeter, it was felt that other controls were unnecessary. Superior collicular lesions were given to P3 to test a hypothesis concerning the origin of the defect caused by frontal eye-field lesions (see Discussion).

The cortical lesions were made by sub-pial aspiration with a narrow gauge sucker. For the frontal eye-field lesions, an attempt was made to remove the region of
cortex defined as the frontal eye-fields in the stimulation experiments of Crosby et al.²⁰, Jampel³⁸, and Brucher¹⁰. For the principalis lesion, a strip of cortex about 1 cm wide was removed along the sulcus principalis. It extended from the anterior limit of the frontal eye-field almost to the frontal pole, and included both banks and the depths of the sulcus.

The collicular lesions were made electrolytically with the animal in a stereotaxic instrument (Kopf, Model No. 1204). A monopolar cathodal electrode was used. It was made from stainless steel insulated with formvar except for a 1.0 mm 45° tip. Power was supplied by a 108 V battery and, to make the lesion, current was increased from 0 to 5 mA over 15 sec, held constant at 5 mA for 30 sec and then reduced to zero again over 5 sec. For the first lesion, on the right side, 13 electrode placements were used (D is the depth from the surface of the cortex in mm):

A —1,  D 24:  L 1.5 L 3 L 4.5
A  0,  D 23:  L 1.5 L 3 L 4.5
A  +1,  D 22:  L 1.5 L 3 L 4.5
A  +2,  D 22:  L 1.5 L 3 L 4.5
A  +3,  D 22:  L 1.5 L 3

On the left side, 3 additional placements were used:
A  —2,  D 24:  L 1.5 L 3 L 4.5

Histology

At the end of the experiment the monkeys were given an overdose of Nembutal and perfused through the aorta with 10% saline followed by formol-saline. Frozen sections were cut at 50 μm and every tenth section saved. These were stained alternately with thionin and according to Weil's method.

Reconstructions of the cortical lesions are shown in Fig. 1. All were close to the intended shape and size, although they generally included more of the posterior end of sulcus principalis than was necessary. In P4, who had a one-stage bilateral frontal eye-field lesion, the most ventral part of both fields was spared although it was partially undercut on both sides. In several cases (P2 right, P3 right, and P4 right) there was a small remnant of cortex left in the angle of the arcuate sulcus, but again this was partially or entirely undercut. In all cases there was some irregular damage to underlying white matter and occasional sparing of deep grey matter. There was no damage to the basal ganglia. Retrograde degeneration, with both gliosis and cell loss, was clearly visible in the dorsomedial nucleus of the thalamus. The extent and site of this degeneration was similar to that described by Akert¹: degeneration after frontal eye-field lesions was limited to pars paramellaris, and after the principalis lesion (P2 left) to pars parvocellularis.

Reconstructions of the collicular lesions given to P3 are shown in Fig. 2. These were smaller than intended, probably because the electrode placements were too high. There was little apparent difference in the size of the two lesions. In both cases, damage was limited to the superficial layers of the colliculus and the lateral, rostral and extreme caudal tissue was spared. The commissure of the superior colliculus was intact. There
Fig. 1. Reconstructions of the cortical lesions in the 4 subjects, with representative sections through the lesion and the region of thalamic degeneration. Lesions and thalamic degeneration are shown in black.

was no mid-brain damage outside the superior colliculi, but there was some electrode tract damage in gyrus precentralis and gyrus cingulate posterior of the cortex. The extent of this was approximately equal on both sides.

Brain Research, 30 (1971) 1–24
RESULTS

Pre-operative training

All monkeys learnt to work the perimeter, though as Table I shows there was considerable variation in the time taken. After 23 months, P2 had stabilised at around 81% correct performance. So he was operated on without achieving the criterion of 90% that was used for the other monkeys.

General post-operative behaviour

The effects of the unilateral frontal eye-field lesions on the monkeys' general behaviour were very marked, but temporary. Apart from differences in laterality, it made no difference whether the lesion was the first or second, and in all cases the gross abnormal behaviour after the first lesion had completely disappeared before the second lesion was made. Ipsilateral head turning and conjugate ipsilateral deviation of the eyes always occurred as soon as the monkeys recovered consciousness,
but never before. After from two to seven days, this was no longer noticeable in the home cage, although it might still be evident in the perimeter. Despite this ipsilateral deviation, contralateral eye movements across the vertical mid-line were observed in all monkeys. Ipsilateral circling, which included head and eye deviation, occurred immediately after all the frontal eye-field lesions except P6's. This was very strong at first and interfered with the picking up of food, but it gradually declined until after several weeks it occurred only occasionally. The most striking properties of this circling were its apparent purposefulness and the variety of ways in which it was achieved. The monkey appeared to be tracking an interesting stimulus that was slowly circling him, and he might for example move on one occasion on all fours and on another by sitting down and twisting himself round with his arms. P6 showed spasmodic circling, but it was much less pronounced than in the other monkeys. Their general activity level, apart from the circling, seemed to be depressed for the first few post-operative weeks. They never misreached for food, but when offered a choice of two peanuts all showed a consistent preference for the one ipsilateral to the lesion. In some cases the contralateral peanut was ignored entirely. They tended to use the hand ipsilateral to the lesion for reaching to either side but, if forced to, they would use the contralateral hand in an apparently normal way. When tested in the home cage, the fear response to a frightening object such as a monkey doll occurred whether the object was present ipsilaterally or contralaterally, though for a few days after the removal of his second, left, frontal eye-field P3 would sometimes overlook the doll when it appeared to his right. Two monkeys with unilateral frontal eye-field lesions that were tested with their heads and bodies restrained showed an almost complete neglect of all objects in the contralateral half-field for about a week after the operation. Orientation and withdrawal responses to auditory and tactile stimuli seemed to be normal for all monkeys.

P4, who had both frontal eye-fields removed at the same operation, showed very few changes in his general behaviour. He seemed less active and less responsive to visual stimuli for about a week, but he could move his eyes and head in every direction and was certainly not blind.

The unilateral principalis lesion given to P2 produced no noticeable effect on his general behaviour.

After each collicular lesion, P3 responded normally to frightening stimuli presented in any part of his visual field, but when two peanuts were held up in front of him he nearly always reached for the ipsilateral one. This lasted for a few days only, and was more marked after the first lesion. His left hand preference was unaffected by either lesion. He showed no eye or head deviation and no forced circling, and when tracking or fixating he seemed to be able to move his eyes equally well in all directions.

All monkeys resumed perimetric testing on either their first or second post-operative days. However, after all the frontal eye-field lesions there was a tendency to perseverate on one of the response levers. This was not found after the collicular or principalis lesions. The perseveration lasted longer after the second frontal eye-field lesion, and initially it was always on the lever ipsilateral to the lesion. P4 (bilateral...
Brain Research, 30 (1971) 1-24
frontal eye-field) began by perseverating on the left lever. After this initial phase, which lasted from two to six days, all the frontal eye-field monkeys switched to perseverating on the opposite lever. (It is for this reason that the phenomenon is called perseveration rather than an ipsilateral hand preference.) This was followed by a brief period of short perseverative runs, generally lasting for less than a testing session. By the tenth post-operative day, the distribution of lever presses had stabilised for all animals to within 15% of equality. Since perseveration on the left lever abolished all false negative errors, and perseveration on the right resulted in a 100% false negative rate, the first block of 500 trials to be analysed was not begun until the distribution of lever presses had stabilised.

**Perimetry after unilateral frontal eye-field testing**

Fig. 3 shows the visual fields of monkeys P3 and P6 plotted immediately before and after their first and second unilateral frontal eye-field lesions. (The convention P3-1 will be used to refer to the first lesion made on P3, P3-2 to the second, etc. The site of each lesion is given in Table I.) In every case there was a strong tendency post-operatively to respond incorrectly to test flashes in the half-field contralateral to the lesion. The frequencies of correct and incorrect responses to stimuli on the left and right of the vertical meridian were compared by calculating $\chi^2$. To
exclude the possibility of asymmetrical disturbances in fixation introducing an arte-
fact by causing test flashes to fall further out into the periphery on one side than the
other, data were considered only for test flashes falling within the fifty degree square
centred on the fixation point. Table II shows the values of $\chi^2$ obtained. Before their
first operations, neither monkey showed an asymmetry in his visual field. Post-oper-
atively, the asymmetries were highly significant. But the asymmetry diminished with time
(see below) so that for P3 it was no longer significant by the time of the second opera-
tion. For P6 the asymmetry was still there at the time of his second operation although,
like P3, his overall performance had returned to above 90% correct. After their
second operations, both monkeys again showed significant asymmetry, although
after P6-2 $\chi^2$ was comparatively small because the monkey continued to make errors
on the side contralateral to the first lesion.

Fig. 4 summarises in graphical form all the visual fields plotted for P3 and P6. These
graphs were drawn by dividing each visual field into three concentric annuli and
plotting the percentage of flashes correctly responded to in the left and right halves
of each annulus, together with the percentage correct for flashes falling on the vertical
meridian (VM). These show that the impairment was both stronger and longer lasting
after the second operation. Two weeks after the first operation both monkeys were
responding above 90% overall. After the second operation, P3 took 5 weeks to return
to 90% and was still showing asymmetry even then, while P6 never exceeded 70% correct
during 13 weeks of testing.
Fig. 5. P6-1 (left frontal eye-field), post-op days 10–13: the effect of dimming the test flash by 1 log unit. a, standard flash, b, dim flash. For explanation of symbols see Fig. 3.

Fig. 4 also shows that the defect is clearly related to the position of the test flash within the impaired half-field. Performance fell systematically as the flashes became more peripheral until, at a mean displacement of 32.5° from the fixation point, only 30–40% flashes were correctly responded to immediately after operation.

The block diagrams beside the visual fields in Fig. 3 show that the number of false positive errors (L) increased by a small but insignificant amount after the first operations (P3-1: $\chi^2 = 2.2, P > 0.05$. P6-1: $\chi^2 = 2.56, P > 0.05$), and by almost as much as the false negatives after the second operations (P3-2: $\chi^2 = 31.9, P < 0.001$. P6-2: $\chi^2 = 123, P < 0.001$). This pattern of errors, shown by the first post-operative visual fields, was repeated in subsequent testing.

The effect of dimming the test flash by one log unit was tested on days 14–16 after P3-1 and days 10–13 after P6-1. Fig. 5 shows the fields for P6-1. In both cases this procedure restored the field defect: false negative errors increased (P3-1: $\chi^2 = 14.8, P < 0.001$. P6-1: $\chi^2 = 6.7, P < 0.01$), while false positive errors remained

*Brain Research, 30 (1971) 1–24*
Fig. 6. P3-1 (right frontal eye-field), post-op days 7–10: the effect of changing the position of the fixation mirror 15° to the left (top) and to the right (bottom). Moving the mirror to the left caused most of the flashes to fall into the intact right half-field. Moving it to the right made them fall chiefly in the neglected half-field. For explanation of symbols see Fig. 3.

constant (P3-1: \( \chi^2 = 0.03, P > 0.05 \). P6-1: \( \chi^2 = 0.04, P > 0.05 \)). A similar test just before their second operation, when both monkeys were performing at above 90% overall, did not affect the frequency of false negative errors (P3-1: \( \chi^2 = 0.39, P > 0.05 \). P6-1: \( \chi^2 = 0.20, P > 0.05 \)). P6 was not tested with the dimmed flashes after his second operation because his performance with flashes of full intensity was too poor for further detriment to appear. Dimming the stimuli failed to impair P3 after his second operation (false negatives: \( \chi^2 = 0.42, P > 0.05 \); false positives: \( \chi^2 = 0.48, P > 0.05 \)), probably because data were not collected until post-operative days 35–37 when his overall performance with normal test flashes had returned to above 90% correct (see Fig. 4). So, after the first operation at least, the severity of the deficit produced by a unilateral frontal eye-field lesion is related to the luminous energy of the test stimulus.

The effect of moving the fixation mirror 15° to the left or right of the centre of the perimeter was tested after P3-1, P6-1 and P3-2. Fig. 6 shows these visual fields...
Fig. 7. P4 (bilateral frontal eye-field lesion): the effect of the lesion on the visual field. Post-operative data were collected on days 12–14. For explanation of symbols see Fig. 3.

Plotted for P3-1. After all 3 lesions, the frequency of false negative errors was significantly higher with the fixation mirror 15° to the side ipsilateral to the lesion than with it 15° to the contralateral side (P3-1: $\chi^2 = 35.4$, $P < 0.001$. P6-1: $\chi^2 = 17.5$, $P < 0.001$. P3-2: $\chi^2 = 38.7$, $P < 0.001$). Moving the fixation mirror did not affect the monkey's head or body position. So it is possible to conclude that the probability of a stimulus being incorrectly responded to after a unilateral frontal eye-field lesion is related to its position relative to the monkey's retina, but not to its position relative to the monkey's body or to its absolute position within the perimeter.

Perimetry after a bilateral frontal eye-field lesion

Fig. 7 shows the visual field on monkey P4 before and after a one-stage bilateral frontal eye-field lesion. There was a significant increase in the number of false negative errors ($\chi^2 = 39.2$, $P < 0.001$) but no asymmetry in the distribution of these
errors between the two half-fields (Pre-op: $\chi^2 = 0.10$, $P > 0.05$. Post-op: $\chi^2 = 0.89$, $P > 0.05$). The summary graph (Fig. 8) shows that P4's visual field varied considerably during the 11 weeks of post-operative testing, but there was no consistent recovery. In every case performance worsened as the test flashes became more peripheral, but the consistent performance of between 65% and 75% correct at a mean displacement of 32.5° was much better than the initial performance of 30-40% correct in response to stimuli of this eccentricity shown by the animals with unilateral frontal eye-field lesions. As with P3-2 and P6-2, there was also a significant increase in false positives ($\chi^2 = 22.6$, $P < 0.001$) which persisted throughout testing.

Dimming the test flash by one log unit had no effect on the visual field pre-operatively ($\chi^2 = 0.07$, $P > 0.05$), but post-operatively it produced a significant increase in errors ($\chi^2 = 5.33$, $P < 0.05$). Since the performance of P4 was so poor post-operatively, we also looked at the effect of increasing the duration of the test flash from 50 to 500 msec. This produced a significant decrease in the number of errors ($\chi^2 = 4.6$, $P < 0.05$). False positives were not affected in either case. So, as with unilateral lesions, the severity of the deficit produced by the bilateral frontal eye-field lesion was related to the luminous energy of the test flash.

Since the deficit in P4 was symmetrical, the effects of changing the position of the fixation mirror were not investigated.

**Perimetry after a unilateral sulcus principalis lesion**

The unilateral sulcus principalis lesion given to P2 had no effect on his visual field ($\chi^2 = 0.017$, $P > 0.05$) although it did produce a significant increase in false positive errors ($\chi^2 = 26.1$, $P < 0.001$) that lasted for 10 days. The distribution of errors between the two half-fields was also unaffected ($\chi^2 = 1.21$, $P > 0.05$).
A month after his left principalis lesion, P2 was given a right frontal eye-field lesion. This produced a large increase in both false positives and false negatives. Overall performance on the perimeter remained at only 60–70% correct for the 13 weeks of post-operative testing. However, the animal also suffered a complete and persistent loss of fixation of the mirror, his eyes deviating to the right, which meant there were insufficient test flashes in the right half-field to allow a comparison of the two half-fields.

**Perimetry after unilateral lesions of the superior colliculi**

Fig. 9 shows the effect of the first collicular lesion given to P3. After both collicular lesions, there were significantly more errors in the half-field contralateral to the lesion than in the ipsilateral field (P3-3: $\chi^2 = 11.3, P < 0.001$. P3-4: $\chi^2 = 22.8, P < 0.001$). In neither case was the field significantly asymmetrical pre-operatively.
Fig. 10. Summary of the effects of unilateral superior collicular lesions on the monkey’s visual field. V.M. = vertical meridian. * = overall performance above 90% correct.

(P3-3: $\chi^2 = 0.003, P > 0.05$. P3-4: $\chi^2 = 0.18, P > 0.05$), although the deficit in the left field after P3-3 was still detectable at the time P3-4 was made. This persistence of the left deficit is apparent in the summary graph (Fig. 10), although overall recovery was rapid after both lesions, with performance returning to above 90% within 10 days. There was no post-operative change in the false positive rate (P3-3: $\chi^2 = 0.49, P > 0.05$. P3-4: $\chi^2 = 0.03, P > 0.05$).

The field defect after P3-4 was rather larger in area than for P3-3 (Fig. 9), perhaps because 3 extra electrode placements were used in making P3-4, although the histology does not show a marked difference in lesion size (Fig. 2). There is no adequate topographical map available of the retinal projection to the monkey’s superior colliculus but, assuming it to be similar to Apter’s map for the cat, the posterior collicular lesions made here are consistent with a peripheral field defect involving both superior and inferior quadrants.

As with the frontal eye-field lesions, dimming the test flash increased the deficit (P3-3: $\chi^2 = 4.14, P < 0.05$. P3-4: $\chi^2 = 14.3, P < 0.001$), without affecting the false positive rate (P3-3: $\chi^2 = 1.39, P > 0.05$. P3-4: $\chi^2 = 0.17, P > 0.05$). With P3-3,
dimming the test flash also caused the defect to spread down into the lower quadrant, which appeared unaffected at full stimulus intensity (Fig. 9).

Changing the position of the fixation mirror after P3-3 altered the visual deficit in the same manner as after frontal eye-field lesions. There were more false negative errors when the mirror was moved to the right than when moved to the left ($\chi^2 = 5.3, P < 0.05$). This effect was not found after P3-4 ($\chi^2 = 0.0002, P > 0.05$), but this is not surprising since data were not collected until days 15 and 16, when the defect was both very small and distributed symmetrically about the vertical meridian (Fig. 10). Fig. 10 also shows that with the normal test flash the deficit became worse as the retinal eccentricity of the flash increased.

**DISCUSSION**

General observation showed the effects of the frontal eye-field lesion to be similar to those of earlier studies (see Introduction), except that there was no evidence of the decreased sensitivity to auditory and tactile stimuli reported by Welch and Stuteville\(^2\). After all unilateral lesions there was a marked, though transient, reduction in responsiveness to visual stimuli in the contralateral half-field, together with an ipsilateral deviation of the eyes and head. The histology showed that these effects were not, as Lashley suggested\(^3\), caused by basal ganglia damage. The comparative lack of disturbance in the general behaviour of the monkey after a one-stage bilateral lesion also confirms earlier findings.

Assuming that an increase in false negative errors ($R_{SN}$) in the perimeter is caused by a field defect — a point that will be discussed later — the findings of the perimetry study can be summarised as follows. Unilateral frontal eye-field lesions produced a contralateral field defect. This was not absolute — at its worst about a third of the test flashes were still being responded to correctly — and is therefore best described as a hemi-amblyopia. Either making the retinal position of the test flash more peripheral or reducing the intensity of the flash aggravated the field defect. False positive errors were unaffected by the lesion.

The effects of the one-stage bilateral frontal eye-field lesion were, in all respects except that of laterality, qualitatively similar to the effects of unilateral lesions. With two-stage bilateral lesions, the second lesion produced larger and longer-lasting effects and an increase in false positive errors, but was otherwise no different from the first lesion. The increase in false positive errors after the second, more disturbing, lesion may reflect a deterioration in learnt discrimination. (In signal detection theory terminology, the monkeys were lowering their decision criteria to cope with the more severe decrease in discriminability after the second lesion.) This effect was also noticed in an earlier study of field defects after unilateral occipital lobectomy\(^4\).

In most cases there was some recovery. For the two unilateral lesions of P3, this recovery was complete and took 2 and 5 weeks respectively. For the other 3 unilateral lesions and the bilateral lesions, some impairment in the visual field was detectable throughout the whole period of post-operative testing of up to 5 months.

The altered response to contralateral test flashes in the perimeter after unilateral
frontal eye-field lesions is almost certainly evidence for a visual field defect. The change was not caused by the ipsilateral deviation of the eyes, for fixation was controlled. A more general behavioural impairment, such as the delayed response deficit, is unlikely because of the normal response to stimuli in the ipsilateral field. Nor can the defect be accounted for by any impairment of contralateral limb responses, for although a right-sided lesion might impair responses on the left lever, thereby producing false positive errors, a left-sided lesion would be expected to have the opposite effect, which it did not. The patterns of false positive errors and the effects of varying the intensity or position of the test flash were always those to be expected of a visual field defect.

The impaired performance in the perimeter of the one monkey with a one-stage bilateral frontal eye-field lesion cannot be attributed so certainly to a visual field defect. Nevertheless, all the properties of the impairment were those expected of a bilateral field defect, and the finding of Cowey and Weiskrantz that a bilateral inferotemporal lesion did not impair performance on the perimeter partially excludes the possibility of a non-specific deficit produced by any bilateral lesion. There were few signs of a field defect in the monkey's general behaviour. But this could be because bilateral amblyopia is more difficult to detect than unilateral, partly because most tests of amblyopia, including the perimeter, depend on a comparison of the two half-fields, and partly because with a complete amblyopia the monkey is unable to compensate by using the good part of his field — he can compensate only by improving his performance in the impaired field. So the discrepancy between the effects of unilateral and bilateral lesions found in earlier studies (see Introduction) probably arises from the testing procedure used rather than from any paradoxical ineffectiveness of bilateral lesions.

We did not attempt to estimate the magnitude of the field defects in terms of a threshold change. However, on a number of occasions during the experiment the effect of dimming a small patch of from 1 to 25 (a quadrant) stimulus bulbs was investigated. Dimming by up to 2 log units had no effect on the hit rate for test flashes provided they fell in normal parts of the visual field. So the threshold increase produced by the lesions must have been greater than 2 log units.

Cowey and Weiskrantz and Cowey had previously used the perimetric technique described here to map visual fields after retinal and occipital lesions. Retinal lesions produced absolute defects, but partial striate cortex lesions or a complete unilateral occipital lobectomy resulted in only partial defects. Their technique of analysis was slightly different from the one used here, so it is not possible to make a direct comparison of the magnitude of the field defects produced by frontal eye-field and occipital lesions. But, considering test flashes falling in the contralateral hemi-annulus covering the visual field from 27.5° to 37.5° from the fixation point, monkeys with frontal eye-field lesions had an initial post-operative hit rate of between 30% and 40%. The one monkey, D-1, with a unilateral occipital lobectomy described by Cowey and Weiskrantz had a hit rate of 39% over the same region for the first few thousand post-operative trials. Because the monkey was recovering slowly over the period of testing, this is an underestimate of his immediate post-operative deficit. Nevertheless,
it suggests that the field defects after frontal eye-field and occipital lobe lesions are initially of the same order of magnitude, although recovery after the latter lesion is considerably slower and the mechanisms underlying the two defects may be completely different.

The contralateral visual field defects produced by the two unilateral superior collicular lesions were less severe than those following either the occipital or the frontal eye-field lesions — the initial post-operative hit rate over the region described in the previous paragraph was 50–60%. There are two possible reasons for this: it might be that superior collicular lesions in general produce rather slight deficits, or it might be that in this experiment only a small proportion of the superior colliculi were destroyed. From the histology (Fig. 2) and the comparatively limited distribution of errors within the contralateral half-fields (Fig. 9), the second seems more likely. It is not clear whether these field defects are dependent on the earlier removal of both frontal eye-fields, or whether they would occur with collicular lesions alone, although the latter is more likely in view of previous reports of transient visual disturbances after bilateral collicular lesions.

The field defects always outlasted the gross abnormalities seen in the monkey’s home cage, and in one case were still detectable when testing was stopped after 5 months. None of the previous studies of frontal eye-field lesions has found impairments that persisted longer than a few weeks. This suggests that though there is usually some genuine recovery, much of the improvement shown in the monkey’s general behaviour is due to behavioural compensation for an enduring disorder. We cannot say whether the recovery that does occur is spontaneous or, like the recovery from striate lesions, depends on visual experience.

These experiments exclude the two explanations for the frontal eye-field visual impairment suggested in the introduction — that the defect is caused either by the ipsilateral deviation of the eyes or by an inhibition of responses to the contralateral side — but they do not suggest a clear alternative. One hypothesis is that normal monkeys make an orienting fixation response to the position where a test flash has just occurred (the flash itself is too brief for them to fixate) and that if this motor response is abolished or degraded by frontal eye-field lesions the animal responds as if no flash had occurred. This suggestion is not supported by the observation that monkeys with frontal eye-field lesions can move their eyes to fixate an object in the contralateral visual field, and that in the perimeter actual eye movements towards the position of a contralateral test flash were seen, even on trials where the animal made a false negative response. A related hypothesis, suggested by electrophysiological recording from single units in the frontal eye-fields, is that the function of the frontal eye-fields is to monitor eye movements, and that in the absence of any monitoring signal the animal responds as if the eyes had not moved and therefore as if the stimulus eliciting the movement had also failed to occur. There are two problems with this hypothesis. The first is that the monkeys were not required to move their eyes towards the position of the test flash in order to respond correctly, and on the majority of trials they did not. To preserve the hypothesis one would therefore have to assume that the frontal eye-fields were monitoring a tendency to move the eyes, which is not
completed because it is unnecessary. Another difficulty is that in the home cage or restraining chair the monkeys rapidly recovered the ability to detect, fixate and then reach for pieces of food presented in the contralateral visual field, at a time when the neglect was still present in the perimeter. However, there is a distinction between the stimuli used in the two testing situations that may have been crucial. In the perimeter, the neglected stimuli were always brief and peripheral (foveal and near foveal flashes were responded to correctly), but in testing outside the perimeter the stimulus persisted long enough for the animal to fixate it. In this case, the need to monitor eye movements would be much less important. It might be that a neglect outside the perimeter only lasts for as long as the eye movement disturbance prevents fixation.

If the function of the frontal eye-fields is to monitor eye movements and modulate the visual system accordingly, perhaps as part of a system for re-setting the visual frame of reference to allow for eye movements as suggested by Bizzi and Schiller, then destroying it should disturb the functioning of the visual system at a lower level. This might occur in the superior colliculus, which receives a monosynaptic projection from the frontal eye-fields and destruction of which, as we have shown, produces a very similar effect to frontal eye-field lesions.

Another striking feature of the frontal eye-field amblyopia is that although it has been repeatedly found in monkeys (see Introduction) and once in chimpanzees, it has been found only rarely in man. Bard and Silberpfennig describe patients with frontal pathologies who neglected contralateral stimuli. Silberpfennig's two cases in particular had symptoms very similar to those reported for monkeys — including a contralateral deviation of the head and eyes. One of these patients described her visual world as moving round her towards the side of the lesion, occasionally causing her to fall in that direction. This instability of the visual world might have been caused by disruption of the mechanism compensating for eye movements which Bizzi and Schiller suggest is located in the frontal eye-fields. Jenkner and Kutschera also describe a patient with pathology apparently limited to the right prefrontal—parasagittal area who had a clear left homonymous hemianopia, although surprisingly he had no oculomotor abnormalities. But in general, studies of patients with frontal pathologies, gunshot wounds, and frontal leucotomies have failed to find visual changes that could not have been accounted for by damage to the visual pathways.

**SUMMARY**

Visual fields of rhesus monkeys were plotted perimetrically with 50 msec flashes, using corneal photography to determine eye position.

Unilateral removal of a frontal eye-field produced a contralateral hemi-amblyopia, or visual neglect, that grew progressively worse towards the periphery of the visual field. After partial or complete recovery, removal of the contralateral frontal eye-field produced an amblyopia in the other half-field that was both more severe and more prolonged than the first. There was always some recovery, which varied.
from a complete recovery after two weeks with one of the first unilateral lesions, to a very slight recovery over five months of testing with one of the second lesions.

A one-stage bilateral frontal eye-field lesion produced an impairment that was consistent with a permanent bilateral amblyopia.

After recovery from a two-stage bilateral frontal eye-field lesion, unilateral lesions in the superior colliculus caused further transient contralateral amblyopias.

The origins of the frontal eye-field amblyopia remain obscure. But it is suggested that the frontal eye-fields might normally monitor eye-position and modulate the visual system accordingly, and that blocking this modulation is sufficient to produce an amblyopia.

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