FIXATION CHANGES AFTER FRONTAL EYE-FIELD LESIONS IN MONKEYS

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INTRODUCTION

The two main effects that have been reported after unilateral frontal eye-field lesions in monkeys are a neglect of contralateral visual stimuli\cite{3,4,9,10,13,16,22} and an ipsilateral deviation of the eyes and head\cite{3,11,13,15,22}. Bilateral lesions, on the other hand, are generally said to have very little effect on either responses to visual stimuli or eye movements. In an earlier paper\cite{16} we reported results obtained using a specially designed perimeter to map the visual fields of monkeys with frontal eye-field lesions. This perimeter also enabled us to analyse the fixations of these monkeys, providing for the first time quantitative data on the disturbances in fixation that are caused by frontal eye-field lesions. These data are the subject of the present paper.

METHOD

Apparatus and procedure

The perimetric apparatus was the same as in the immediately preceding paper\cite{16}. As described there, each monkey was trained to look with his right eye through a 2 cm circular peep-hole at a hemispherical perimeter containing stimulus bulbs set at 5° intervals. The centre of the perimeter lay 20° above the horizontal straight-ahead position of the animal’s viewing eye. At this central position was a 2° plane mirror aligned so that the animal saw a reflexion of his own eye when he fixated it. The monkey’s task was to fixate the mirror and wait for a stimulus to be delivered by the experimenter. The stimuli were of two kinds — either a 50 msec click plus a coincident 50 msec flash of light from any one of the perimeter bulbs, or the click alone. The animal was rewarded for pressing a lever to his left in response to the paired stimulus and for pressing a lever to his right in response to the click alone. His viewing eye was

photographed with a single exposure, synchronised with the stimulus, on every trial. This enabled the direction of fixation to be determined afterwards, as described in the previous paper. 

Pre-operatively the monkeys were trained to fixate the mirror by attempting to withhold the stimulus until they did so. This was a straightforward procedure since they all had a strong tendency to look at the mirror, and it was only necessary to prevent this behaviour from extinguishing. It was of course impossible for the experimenter to know whether the animal was looking precisely at the mirror rather than at some point close to it, but for any trial the actual locus of fixation was determined afterwards from the eye photograph. It was also impossible to prevent any sudden and large change in fixation just prior to presenting a stimulus. Stimulus presentation was therefore not completely dependent on accurate fixation of the mirror.

During post-operative testing the stimulus was delayed for a few seconds if fixation did not occur, but was then presented in the normal way. So a failure to fixate did not on its own reduce the number of trials, and therefore the number of rewards obtainable, although it did lengthen the trials. However, when combined with certain kinds of field defect a change in fixation could impair overall performance in the perimeter, for instance by causing more of the light flashes to fall within a contralateral field defect, see Discussion.

Eye movements, as opposed to fixation, were observed in all monkeys by placing the animal in a restraining chair and eliminating all but slight head movements with an adjustable padded frame fitting round the sides, back and top of the head. The chair was then placed inside a chamber with sides made of black cloth. This contained a horizontal slit through which the experimenters could introduce objects such as an apple or small furry monkey doll into the animal's visual field. Eye movements in response to the stimulus were observed through a peep-hole.

Subjects

The subjects were 6 immature male rhesus monkeys. Details of their lesions are given in the previous paper. Two monkeys (P6 and P3) were given two-stage bilateral frontal eye-field lesions and their fixation was studied before and after removing each eye-field. Monkey P3 then received a two-stage bilateral lesion of the superior colliculus. One monkey (P2) received a unilateral lesion of the left sulcus principalis followed by removal of the right frontal eye-field, and one (P4) was given a single-stage bilateral frontal eye-field lesion. In addition two monkeys (N1 and N2) were given unilateral frontal eye-field lesions. They were not tested in the perimeter, but their eye movements were observed while they were in the restraining chair.

In every case where more than one lesion was made we waited until any changes in fixation caused by the first lesion had either disappeared or stabilised before making a subsequent lesion. In describing the consequences of serial lesions in a single animal, e.g. P3, the convention P3-1 is used to refer to the first lesion, P3-2 to the second, etc.
RESULTS

Unilateral frontal eye-field lesions

Gross behaviour. All monkeys in this group, whether the lesion was the first to be made or whether it was made after recovery from a previous lesion, showed marked conjugate deviation of the eyes and head turning, both ipsilateral, as soon as they recovered consciousness after the operation, together with the contralateral visual neglect described in the previous paper. But contralateral eye movements were seen occasionally in all monkeys. This behaviour in the home cage was confirmed by more systematic testing in the restraining chair. With the monkey's head held, moving objects introduced into the peripheral visual field contralateral to the lesion were rarely fixated until they reached the vertical meridian and crossed into the ipsilateral half-field, when they were immediately tracked. Objects introduced into the ipsilateral periphery were almost always fixated immediately and tracked, and this tracking usually continued as the stimuli moved over the midline of the head onto the contralateral side. But when the eyes were deviated contralaterally in this

![Graph showing the effect of lesions on the percentage of trials in which the mirror was accurately fixated.](image)

Fig. 1. The effect of the lesions on the percentage of trials in which the mirror was accurately fixated. Note the three different time scales along the abscissa. P3-1, Right frontal eye-field; P3-2, left frontal eye-field; P4, bilateral frontal eye-field; P3-3, right superior colliculus; P3-4, left superior colliculus; P6-2, right frontal eye-field; P6-1, left frontal eye-field; P2-1, left sulcus principalis; P2-2, right frontal eye-field.

Brain Research, 30 (1971) 25–36
Fig. 2. The effect of P3-1 (right frontal eye-field lesion) on accuracy of fixation. The concentric circles show displacement from the fixation mirror in 5° intervals. Solid circles show the positions where fixations occurred. The area of these solid circles is proportionate to the number of fixations at that position. The positions of fixations outside the inner square are only approximate, since they fell outside the area for which we had standard reference photographs.

way they commonly flicked back to the primary position, and remained there even though the stimulus was still present; and one monkey, two days after his second, right frontal eye-field was removed, consistently failed to track stimuli as they moved across the midline into the contralateral side. So although there was no doubt that contralateral eye movements did occur, they were less frequent and less sustained than ipsilateral movements. Furthermore, since they occasionally occurred when no stimulus had been presented, the rare instances referred to above when the animal did fixate a stimulus introduced into the contralateral peripheral field may have been a consequence of a fortuitous eye movement to that side rather than a direct response to the stimulus. In every case these gross oculomotor abnormalities disappeared about a week after the operation.

Fixation changes. Fig. 1 shows the effect of all the lesions on accuracy of fixation. All the unilateral frontal eye-field lesions were followed by a drop in the number of trials on which the mirror was fixated. Figs. 2–5 show the immediate post-operative changes in monkeys P3 and P6 in more detail. After all 4 frontal eye-field lesions there
Fig. 3. The effect of P3-2 (left frontal eye-field lesion) on accuracy of fixation. (For explanation of symbols see Fig. 2.)

Fig. 4. The effect of P6-1 (left frontal eye-field lesion) on accuracy of fixation. (For explanation of symbols see Fig. 2.)
Fig. 5. The effect of P6-2 (right frontal eye-field lesion) on accuracy of fixation. (For explanation of symbols see Fig. 2.)

Fig. 6. The effect of P2-1 (left sulcus principalis lesion) on accuracy of fixation. (For explanation of symbols see Fig. 2.)
was a tendency for the direction of gaze to be shifted downwards and to the side of the perimeter ipsilateral to the lesion. This displacement was larger after the second lesion, and reference to Fig. 1 shows that it also lasted longer. This was particularly marked after P6-2, for when testing was stopped 91 days post-operatively only 81% of fixations were on the mirror, compared with 97% immediately before the second operation. And in all cases, the tendency for ipsilateral fixations in the perimeter persisted long after there was no sign of a conjugate deviation of the eyes in the home cage or in the restraining chair.

Monkey P2 was initially given a lesion in the region of his left sulcus principalis. Figs. 1 and 6 show that this had no effect on his accuracy of fixation in the perimeter.

A month after the left principalis lesion, P2 received a right frontal eye-field lesion. This produced a striking change in fixation that persisted over the 13 weeks of post-operative testing (Fig. 1). The direction of gaze was shifted downwards and to the right to a point about 25° from the fixation mirror (Fig. 7). The size and direction of this shift remained remarkably constant.

Bilateral frontal eye-field lesion

Monkey P4, who had a one-stage bilateral frontal eye-field lesion, showed no obvious oculomotor abnormalities on gross observation in the home cage or restraining
Fig. 8. The effect of P4 (bilateral frontal eye-field lesion) on accuracy of fixation. (For explanation of symbols see Fig. 2.)

Fig. 9. The effect of P3-3 (right superior colliculus) on accuracy of fixation. (For explanation of symbols see Fig. 2.)
chair. There was possibly a slight reduction in the number of eye movements made, but there was no doubt that he could make both saccades and pursuit movements in all directions.

Despite this, fixation in the perimeter was considerably altered (Figs. 1 and 8). There was a strong tendency to look about 25° below and slightly to the right of the fixation mirror, which persisted throughout 11 weeks of post-operative testing, although towards the end it varied considerably in magnitude.

*Unilateral lesions of the superior colliculi*

Although the two-stage superior collicular lesion made in P3 led to unilateral neglects similar to those produced by the earlier frontal eye-field lesions, they did not produce conjugate deviation of the eyes and from gross observation they did not affect tracking or fixation. Neither did they affect accuracy of fixation in the perimeter (Figs. 1, 9 and 10).

**DISCUSSION**

The ipsilateral deviation of the eyes found in the perimeter after unilateral
frontal eye-field lesions confirms what has been found before with gross observation. However, it persisted in the perimeter long after there was no oculomotor change evident on gross observation, and in the worst case (P2-2) there was no recovery over 4 months of testing. It seems very unlikely that there was rapid and total recovery in the home cage and not in the perimeter, and the simplest conclusion is that fixation changes of up to $20^\circ$ are not detectable by examining the animal in the home cage, where he constantly moves his head and body as well as his eyes.

After recovery from a unilateral lesion, removal of the second frontal eye-field produced a larger and longer lasting deviation in the opposite direction. In addition, after both unilateral and one-stage bilateral lesions, monkeys looked below the fixation mirror. It was as if the removal of the frontal eye-fields produced an impairment with two components: a tendency for the eyes to remain in their primary, straight-ahead position, which was well below the fixation mirror, and, with unilateral lesions only, an additional ipsilateral horizontal deviation. These fixation changes are unlikely to be a simple consequence of the kind of field defect described in the previous paper. Similar field defects after unilateral striate cortex lesions are associated with contralateral, not ipsilateral, deviations, while collicular lesions produce a field defect without affecting fixation. The ipsilateral deviation produced by the unilateral frontal eye-field lesions is actually maladaptive in the perimeter, for it moves more of the test flashes into the impaired, or neglected, half-field.

The most probable origin of the lateral deviation is an imbalance in the oculomotor system. Stimulation of a particular point in the frontal eye-field produces an eye movement along a well-defined vector that always has a contralateral horizontal component. This is effected by contraction of the contralateral lateral recti and ipsilateral medial recti, together with relaxation of the ipsilateral lateral recti and contralateral medial recti. It is unlikely, though not impossible, that the frontal eye-fields are in any sense a primary control centre for saccades leading to fixation, for apart from a transient gross impairment the animals were able to look towards objects presented to them outside the perimeter after removal of one or both eye-fields. Also, single units in the frontal eye-fields have so far been found to respond only after the start of an eye movement and, anatomically, there is probably no direct connection with the eye muscle nuclei, though this is disputed by Crosby. But if we assume that the frontal eye-fields exert a tonic influence on the oculomotor system, perhaps through the strong projection to the superior colliculus or through the mesencephalic reticular formation, then removal of one eye-field could produce an imbalance in the oculomotor system sufficient to cause a lateral deviation. If this supposition is correct, removing the second eye-field before recovery from removal of the first would cause fixation in the perimeter to return towards the mid-vertical position.

The tendency for the eyes to remain in their primary straight-ahead position after a one-stage bilateral frontal eye-field lesion could be caused by a reduction in eye movements that are not a direct response to a visual stimulus, for the inside of the perimeter was comparatively homogeneous visually. Traditionally, the frontal eye-fields have been thought to be involved in voluntary or searching eye movements.
although there is little experimental evidence for the idea. A second possibility, which unfortunately was not tested, is that the animal fixated eccentrically and below the mirror by an amount which coincidentally brought its eyes close to the primary straight-ahead position. If so, raising or lowering the mirror should lift or lower the eyes from the primary straight-ahead position.

A further and consistent finding in this and in the previous paper\textsuperscript{16} is that the fixation changes and field defects lasted longer after the second frontal eye-field lesion. This difference would be trivial were the second lesion always larger than the first, but there is no indication that this was so. It is more likely that a remaining frontal eye-field participates in the recovery from the effects of removing the first, and the very enduring defects caused by a single-stage bilateral lesion are consistent with this view.

**SUMMARY**

Rhesus monkeys were trained to look through a peep-hole and fixate a 2° mirror which showed a reflexion of their own eye. Their direction of gaze was determined to the nearest 3.5° using corneal photography, and the accuracy with which they fixated the mirror was plotted pre- and post-operatively.

Unilateral frontal eye-field lesions produced a consistent, though usually transient, shift in fixation of up to 10° to the ipsilateral side. On recovery, removal of the second eye-field produced a larger (up to 20°) and longer lasting shift in the opposite direction. Both unilateral and one-stage bilateral lesions also produced a downward shift in fixation of up to 25°, with the monkey’s eyes tending toward the primary, straight-ahead position. These fixation changes persisted after there was no oculo-motor change evident on gross observation, and in the worst case there was no recovery over 4 months of testing.

Additional unilateral lesions of the superior colliculus, or a unilateral lesion of sulcus principalis, had no effect on fixation.

These changes in fixation suggest that the frontal eye-fields normally exert at least a tonic influence on the eye muscle nuclei.

**REFERENCES**

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