

Visual neglect in the monkey

Representation and disconnection

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Summary

Macaque monkeys were trained preoperatively in a visual search task. Neglect after a unilateral lesion was measured as the tendency to make errors (choices of non-target stimuli) ipsilateral to the lesion. Neglect was observed after optic tract section combined with forebrain commissurotomy ($n = 6$) and after parietal leucotomy, i.e. unilateral section of the white matter between the fundus of the intraparietal sulcus and the lateral ventricle ($n = 3$). Neglect was not observed after optic tract section alone, or forebrain commissurotomy alone, or posterior parietal cortical ablation, or posterior parietal ablation plus frontal eye-field ablation, or after frontal lobectomy plus forebrain commissurotomy ($n = 3$ in each of these groups). We propose that the cortex of each hemisphere maintains a retinotopically organized representation of the visible half-world that is contralateral to the animal's current point of

fixation, and that this representation is based not only on analysis of the current retinal input but also on memory. Visual neglect reflects an impairment in this representation. According to this proposal, the fact that neglect is not caused by optic tract section alone is explained by the ability of the blind hemisphere to build a memory-based representation of what is contralateral to the current point of fixation, using memories of visual information which arrived from the ipsilateral visual field in previous fixations that were directed contralateral to the current fixation point. However, neglect does follow when unilateral optic tract section is combined with forebrain commissurotomy, even though the cortex is intact, because then the blind hemisphere is not only deprived of information arriving from the contralateral field but it is also cut off from information arriving from the ipsilateral visual field, and therefore cannot build a memory-based representation of the currently contralateral visible world.

Keywords: disconnection; memory based representation; monkey; visual neglect

Abbreviations: FC = forebrain commissurotomy (group); FE = frontal eye-field cortex removal (group); FL = frontal lobectomy (group); OT = optic tract section (group); PL = parietal leucotomy (group); PP = posterior parietal cortex removal (group)

Introduction

Neglect is frequently observed in patients with unilateral cerebral lesions, usually in the right hemisphere. In the visual modality, these patients fail to notice objects on the side opposite to the lesion. Despite an extensive literature there is no general agreement as to the cause of neglect, either in the sense of identifying the necessary and sufficient lesion which produces it, or in the sense of understanding the consequent deficit in information processing. One aspect of this failure is that no convincing experimental model of neglect has been produced in monkeys. Our purpose in the present investigation was to take some ideas about neglect arising from recent clinical studies, and to apply them to a new experimental model of neglect in monkeys.

Hornak (1995) studied eye movements in neglect patients. These patients exhibited drawing neglect, that is, when asked to copy a drawing of a left–right symmetrical object such as a butterfly they omitted to include the left half. It was found that when the patients inspected incomplete drawings of this kind, they consistently failed to fixate the missing parts of the drawings; similarly, when inspecting complete drawings of symmetrical objects, they never fixated the left half. When inspecting asymmetrical objects which could not be identified from the right half alone, however, the patients did fixate the left half, showing that their neglect did not simply reflect an oculomotor impairment. From these and other findings Hornak (1992, 1995) concluded that neglect patients ‘have a

poor internal representation of space to the left of their current direction of gaze' (Hornak, 1995, p. 323).

This representational hypothesis of neglect implies that not only the perceptual analysis of current retinal input, but also the retrieval of visual memory, is organized in a retinotopic fashion. If so, then visual neglect should be produced by depriving one hemisphere of all visual input, so that visual memories can no longer be laid down or retrieved in that hemisphere. That can be achieved experimentally by combining unilateral optic tract section with forebrain commissurotomy (section of the corpus callosum and anterior commissure), since this combination of lesions disconnects one hemisphere from both halves of the retinas. The main initial purpose of the present experiment was to measure visual search in monkeys with this combination of lesions. We also measured visual search in monkeys with optic tract section alone. Although hemianopic, such monkeys should not show neglect since the affected hemisphere can build a representation of the visible world which is currently in the blind half-field, by retrieving memories of visual information which was acquired from previous fixations that were further contralateral than the current fixation. It is well established clinically that hemianopia can occur without neglect (Critchley, 1953). Similarly, we measured visual search in monkeys with forebrain commissurotomy alone, to control for the possibility that abnormalities in the group with the combined lesion could be due to forebrain commissurotomy alone.

A further group of monkeys had unilateral ablation of the cortex in the posterior parietal lobe, subsequently combined with unilateral ablation of the pre-arcuate cortex of the frontal eye-field in the same hemisphere. It has been suggested that neglect can be caused clinically by focal cortical lesions in the posterior parietal lobe, particularly in the intraparietal sulcus (Denny-Brown and Chambers, 1958; Mesulam, 1981). However, experimentally produced ablations of posterior parietal cortex in monkeys have seemed to produce only mild and transient effects, which have been described as not comparable in severity to human neglect (Denny-Brown and Chambers, 1958; Heilman *et al.*, 1970; Lamotte and Acuna, 1978; Mesulam, 1981; Lynch and McLaren, 1989; Deuel and Farrar, 1993; Watson *et al.*, 1994). Similarly, the idea that neglect can be caused by lesions in the frontal eye-field (Chain *et al.*, 1972) has received some support from experimental studies in the monkey, but again with the qualification that the effects seen seem to be milder and more rapidly transient than neglect in man (Welch and Stuteville, 1958; Watson *et al.*, 1978; Crowne *et al.*, 1981; Rizzolatti *et al.*, 1983; Deuel and Farrar, 1993). These earlier studies raise the problem of quantifying the severity of neglect in monkeys in such a way as to permit comparison with the severity of human neglect. In the present study the effect of unilateral posterior parietal ablation, subsequently combined with frontal eye-field ablation, was compared quantitatively with the effect of optic tract section alone. If the effects of a unilateral lesion are no more severe than the effect of

hemianopia (optic tract section alone), we may conclude that they are not comparable to human visual neglect. Thus, the behaviour of monkeys with optic tract section alone can be used as a benchmark to decide whether the changes seen after some other manipulation are sufficiently severe as to be analogous to human neglect.

Also included in the study were a group of monkeys with unilateral frontal lobectomy combined with forebrain commissurotomy, and a group with unilateral parietal leucotomy, i.e. unilateral section of the white matter between the fundus of the intraparietal sulcus and the lateral ventricle. The interpretation of the findings from these groups is taken up in the Discussion. The animals in all of the groups were trained to perform the visual search task without errors preoperatively, and were then assessed in the same task after each surgical operation.

Methods

Subjects

These were 15 adult male macaque monkeys, eight rhesus (*Macaca mulatta*) and seven cynomolgus (*Macaca fascicularis*). The individuals are identified as S1–S15 in Table 1; S6, S9, S10, S11, S13, S14 and S15 were cynomolgus and the remainder were rhesus. Before beginning the present experiment every monkey had served as a normal control in previous experiments involving visual learning in a touch-screen apparatus similar to that described below.

Surgery

The surgery and experiments were all performed under licence from the Home Office, UK. After completing the preoperative training program described below, each monkey was operated upon either once or twice, with recovery and postoperative testing after each surgical operation. The hemisphere in which the unilateral operation was carried out is shown in Table 1 (*see Results*) by L (left) or R (right) for each monkey. The surgical procedures are identified in the table, and in Figs 4 and 5, by group labels as follows. Group PP had unilateral removal of posterior parietal cortex. Group PP+FE had unilateral removal of posterior parietal cortex plus, in the same hemisphere, unilateral removal of prearcuate cortex in the frontal eye-field. Group OT had unilateral optic tract section. Group FC had forebrain commissurotomy. Group OT+FC had unilateral optic tract section plus forebrain commissurotomy. Group PL had unilateral parietal leucotomy. Group FL+FC had unilateral frontal lobectomy plus forebrain commissurotomy. In the case of the monkeys which were operated upon twice, the order in which the two operations were performed can be seen in Table 1. For example, monkey S4 appears once in Group OT and subsequently in Group OT+FC, while monkey S7 appears once in Group FC and subsequently in Group OT+FC.

All the operations were carried out under aseptic conditions

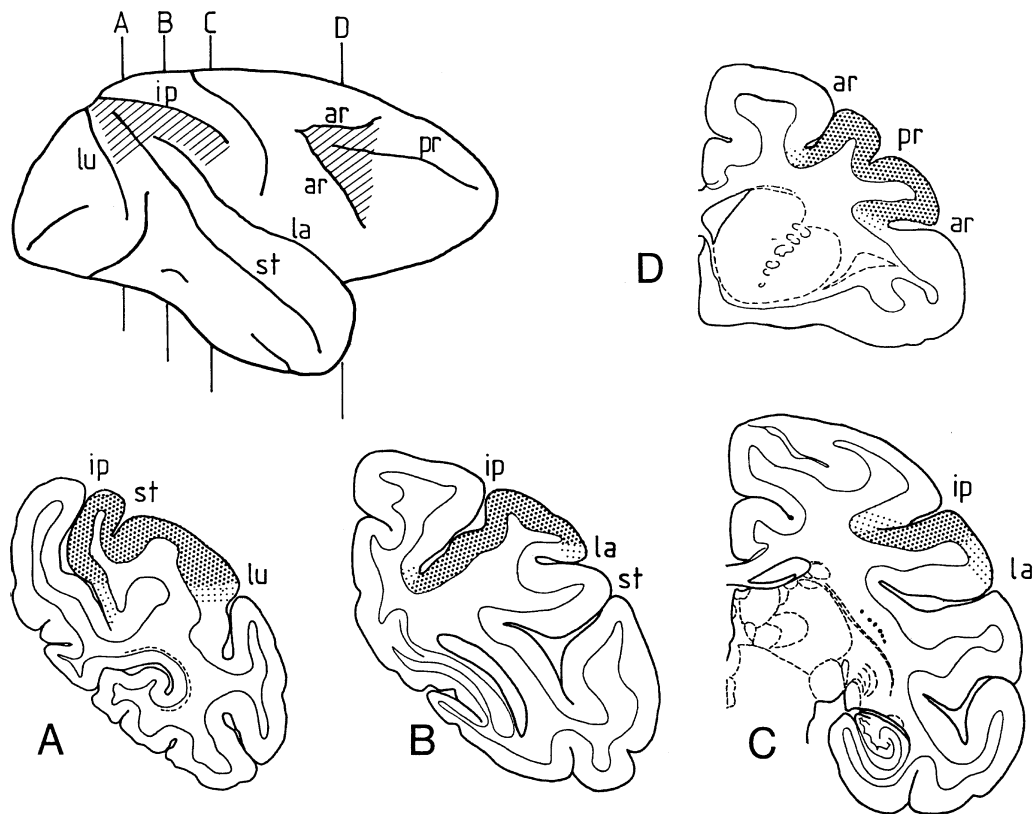


Fig. 1 The extent of cortical ablations in the animals with ablation of the posterior parietal cortex and the frontal eye-field. The cortex removed is shown on drawings of a normal brain. *Upper left*: the external appearance of the hemisphere in a lateral view, posterior to the left and anterior to the right. The areas ablated are shown by cross-hatching. The letters A, B, C and D show the planes of four coronal sections, in which the area that was ablated in all three monkeys is shown by heavy stippling, and the areas that were ablated in at least one but not all monkeys are shown in light stippling. Abbreviations: lu = lunate sulcus; ip = intraparietal sulcus; st = superior temporal sulcus; la = lateral sulcus; ar = arcuate sulcus; pr = principal sulcus.

with the aid of an operating microscope, and the monkeys were anaesthetized throughout each operation with barbiturate (thiopentone sodium) administered through an intravenous cannula. At the end of each operation the dura mater was sewn, a bone flap was replaced in the skull, and the wound was closed in layers. After each surgical operation the animal rested for 17–21 days before resuming the behavioural task. The details of the surgical procedures were as follows.

Posterior parietal cortex removal

A bone flap was raised over one parietal lobe and the dura mater was cut to expose the surface of the lobe. The pia mater was cauterized and cut round the visible limits of the ablation on the surface of the lobe. A metal aspirator was then used to remove cortical tissue and pia mater within the intended limits of the ablation. The ablation is illustrated in Fig. 1. It included the entire lateral bank of the intraparietal sulcus, and extended laterally from the inferior part of the intraparietal sulcus to the lip of the lateral sulcus. Posterior to the tip of the lateral sulcus the ablation extended from the intraparietal sulcus to the lip of the lunate sulcus, and

included both banks of the most posterior part of the superior temporal sulcus.

Precarcuate cortex removal in the frontal eye-field

The method was similar to the posterior parietal removal. The ablation is illustrated in Fig. 1. The tissue removed was in the cortex anterior to the arcuate sulcus, including the entire anterior bank of the arcuate sulcus together with the cortex on the surface of the lobe and within the principal sulcus, up to the anterior limit of a line drawn between the tips of the ascending and descending limbs of the arcuate sulcus. In all cases the precarcuate removal was in the same hemisphere as the posterior parietal removal.

Optic tract section

A bone flap was raised over the dorsolateral frontal lobe on one side, extending to the brow anteriorly, within 2–3 mm of the midline medially, and to the lateral sulcus laterally. The dura mater was cut over the dorsolateral surface of the frontal lobe. The frontal lobe was gently retracted from the

posterior surface of the orbit of the eye with a brain spoon that was inserted between the dura mater and the pia mater. The optic tract was visualized posterior to the sphenoid bone, immediately lateral and posterior to the optic chiasm. The tract was cut with electrocautery and aspiration under visual guidance.

Forebrain commissurotomy

A bone flap was raised over the midline. The dura mater was cut to expose one hemisphere up to the midline. Veins draining into the sagittal sinus were cauterized and cut. The hemisphere was retracted from the falx with a brain spoon. The corpus callosum was sectioned with a glass aspirator in the midline throughout its anterior–posterior extent. The fornix was retracted and the third ventricle was entered from the lateral ventricle with a narrow brain spoon (3 mm wide) in order to section the anterior commissure by cautery and aspiration with a thin metal aspirator (23 gauge) that was insulated to the tip. Coronal sections showing an optic tract section and a forebrain commissurotomy are shown in Fig. 2.

Parietal leucotomy

A bone flap was raised over the midline and one parietal lobe. The lateral ventricle was first located by retracting one hemisphere from the falx at the splenium of the corpus callosum and sectioning the callosum with a glass sucker 2–3 mm lateral to the midline. Next the pia mater was cauterized over the lateral-posterior bank of the intraparietal sulcus, and the cortex in the lateral-posterior bank of the sulcus was removed to expose the white matter at the fundus of the intraparietal sulcus. The white matter was sectioned by electrocautery and aspiration, along the line of the intraparietal sulcus and towards the lateral ventricle, until the lateral ventricle appeared. Section through white matter into the lateral ventricle was continued laterally to the tip of the lateral sulcus. The lateral ventricle served as a landmark to guide the cut and to limit its extent ventrally. A parasagittal section through a parietal leucotomy is shown in Fig. 3.

Frontal lobectomy

A bone flap was raised over the midline and one frontal lobe. All the cortex in the frontal lobe was removed, including the dorsolateral and orbital surface of the lobe and the cortex on the medial surface of the lobe, but the primary motor cortex was spared. The posterior limit of the ablation was the superior precentral dimple, which lies in the cortex between the central sulcus and the ascending limb of the arcuate sulcus, and a line drawn at a right angle to the midline through the precentral dimple from the corpus callosum to the lateral sulcus. Thus, all the cortex in both banks of the arcuate sulcus was removed. The lateral limit of the ablation was the lateral sulcus, which also limited the ablation posteriorly on the orbital surface of the frontal lobe. Medially

the ablation was continued to the corpus callosum, which was sectioned in the same operation as part of forebrain commissurotomy, and ventrally below the genu of the corpus callosum to remove the whole of the gyrus rectus.

Histology

After the completion of behavioural experiments the animals were sedated and deeply anaesthetized and perfused through the heart with saline followed by formol–saline solution. The brains were blocked in the coronal stereotaxic plane, removed from the skull, allowed to sink in sucrose-formalin solution, and sectioned at 50 μ m on a freezing microtome. The brains were sectioned coronally except for those with a parietal leucotomy (S10–S12), which were sectioned parasagittally. Every tenth section through the area of the ablations was retained, mounted on glass and stained with cresyl violet.

Figure 1 shows the extent of the cortical ablations in the animals with unilateral removals of the posterior parietal cortex and the frontal eye-field (S1–S3). For convenience, the removals are illustrated as if they were all in the right hemisphere, though in one case (S3) they were in the left. The cortex which had been removed from these brains is shown reconstructed on sections drawn from a normal brain. The removals were complete in every case.

Figure 2 shows illustrative sections from one of the subjects in the group with optic tract section and forebrain commissurotomy (S4–S9). Microscopic examination of the stained sections from this group confirmed that in every case the optic tract, the corpus callosum and the anterior commissure were sectioned. Unintended damage was limited to the fornix and the medial septal area, both of which were slightly damaged at the site of the anterior commissure section.

Figure 3 illustrates parietal leucotomy (S10–S12). In each case the incision in the white matter inferior to the intraparietal sulcus extended into the lateral ventricle, as intended. In every case cell loss was noted in the lateral geniculate nucleus in the leucotomized hemisphere, indicating that the optic radiations had been damaged.

Examination of the stained sections from the animals in the group with frontal lobectomy and forebrain commissurotomy (S13–S15) indicated that in every case the frontal cortex was removed unilaterally up to the posterior limit of the precentral dimple. Section of the corpus callosum and anterior commissure in these animals was similar to that described above for the animals in the group with combined optic tract section and forebrain commissurotomy.

Apparatus

The monkey was brought to the training apparatus in a wheeled transport cage (floor area 600 mm wide and 500 mm deep), which was then fixed to the front of the apparatus. The monkey could reach out through bars at the front of the transport cage to touch a touch-sensitive colour monitor screen which

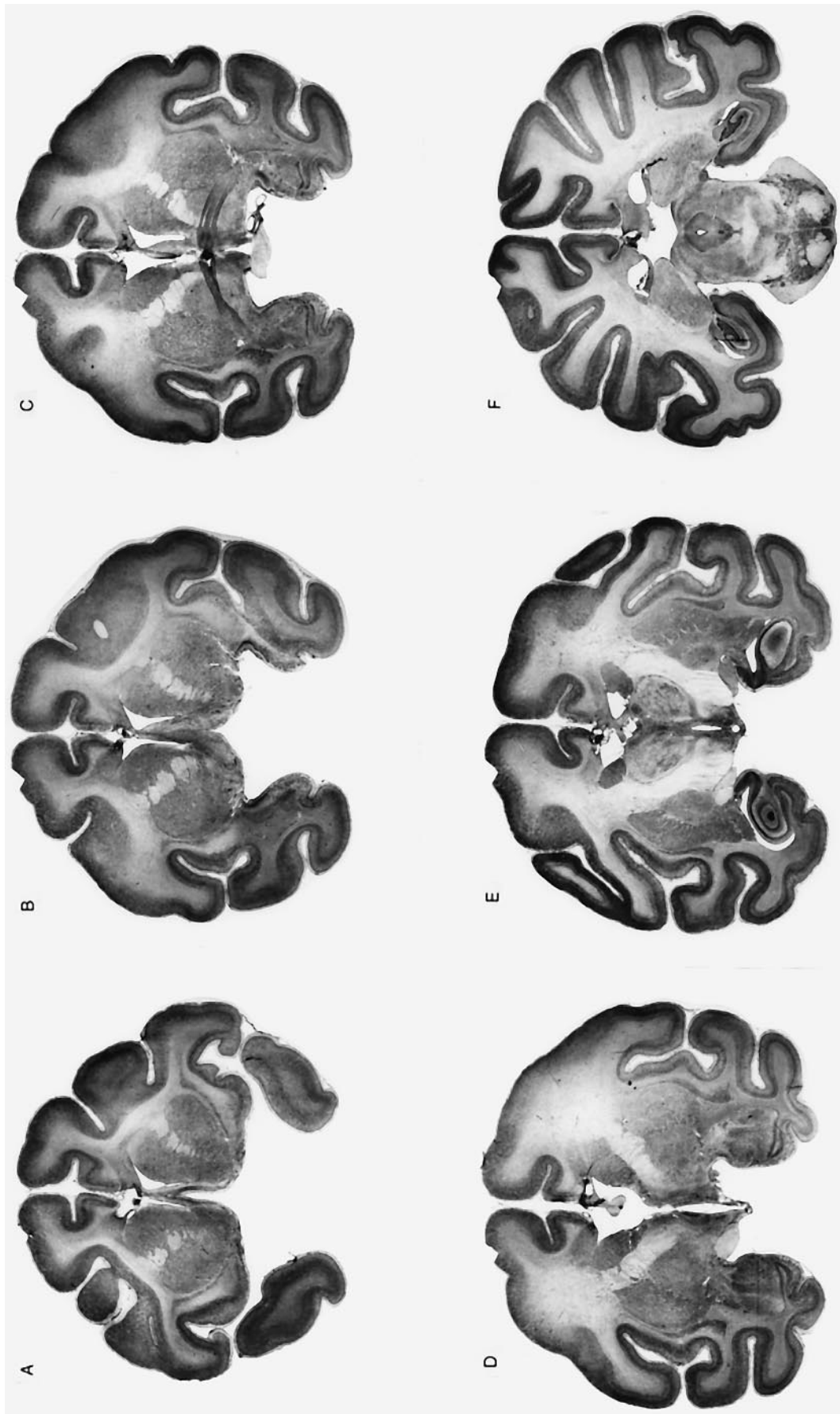


Fig. 2 Coronal sections through the brain of an animal with optic tract section plus forebrain commissurotomy. The most anterior section is labelled **A** and the most posterior **F**. In section **D** it can be seen that the optic tract, at the base of the brain near the midline, is present in the left hemisphere (shown on the left) but not in the right hemisphere. The corpus callosum is sectioned throughout its extent, from the genu (**A**) to the splenium (**F**). In section **C**, the anterior commissure is cut in the midline.

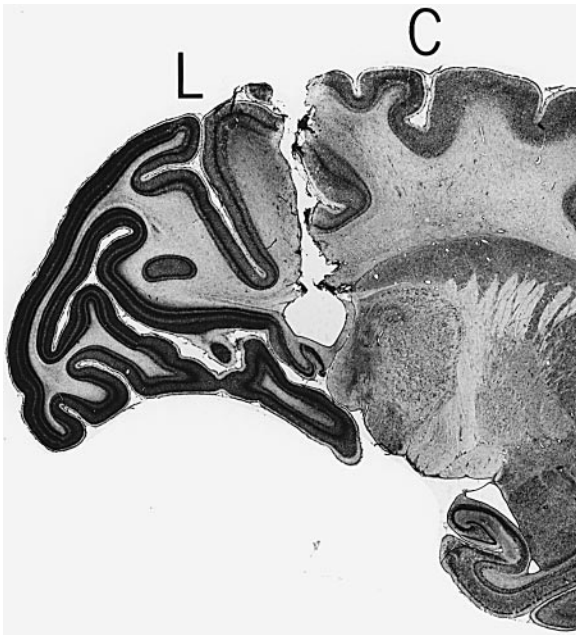


Fig. 3 A parasagittal section through the brain of an animal in the group with parietal leucotomy. The occipital lobe is to the left. The frontal lobe anterior to the arcuate sulcus is not shown. For description, see the text. L = lunate sulcus; C = central sulcus.

was 150 mm from the front of the cage. The screen was 380 mm wide and 280 mm high. A closed-circuit television system allowed the experimenters to watch the monkey from another room, and the room with the monkey and apparatus contained no other monkeys or people during the test sessions. Small food rewards (pellets specially formulated for monkeys, 190 mg) were delivered into a hopper placed centrally underneath the monitor screen. A single large food reward was delivered at the end of each training session by opening a box which was set to one side of the centrally placed hopper. The box contained peanuts, raisins, proprietary monkey food, fruit and seeds. The amount of this large reward was adjusted for individual animals in order to avoid obesity. Opening of the box with the large food reward, like all other aspects of the events and the experimental contingencies during any session of training, was under computer control. The small and large rewards dispensed in the training apparatus provided the whole daily diet of the monkeys on days with a test session.

Stimulus material

The stimuli displayed to the monkey on the monitor screen were unique coloured patterns created by superimposing a small typographic character in one colour onto a larger different typographic character of a different colour. The typographic characters were from several available fonts and included typographic marks such as the interrogation point as well as alphanumeric characters. In total 576 discriminably different typographic characters were available. Thus, for example, one of the patterns consisted of a red Gothic capital M with a cyan curly bracket superimposed on it. The patterns

were on average 20 mm high and 20 mm wide. There were 30 unique positive (rewarded) patterns and for each one of those there were 14 unique negative (unrewarded) patterns. At the beginning of the experiment the 450 stimuli (30 sets, each consisting of one positive and 14 negative stimuli) were selected at random, without replacement, from the large population of possible patterns. All 14 of the negative patterns assigned to each positive pattern were used in preoperative testing, but a subset of only four of those negative patterns was used for each positive pattern in the postoperative phase of testing. In the entire postoperative phase of the experiment, any positive pattern was presented with four of its negative patterns, the same four on every trial with that positive pattern. The five stimuli were displayed in a horizontal row centred vertically on the screen with a centre-to-centre horizontal separation between adjacent patterns of 65 mm. Throughout the preoperative phase of the experiment there were three such horizontal rows of five possible positions, arranged one above another on the screen to make 15 possible positions. On every trial the spatial position of the patterns was randomly determined, with the constraint that, within each block of successive trials, each possible spatial position was occupied once by a positive pattern. Thus, there were 15 trials per block in preoperative testing and five trials per block in postoperative testing, corresponding to the total of possible spatial positions in each phase. The positive patterns and their associated sets of negative patterns were used in rotation in the trials of each session, the first of the 30 sets appearing on trials 1, 31, 61, and so on, the second on trials 2, 32, 62, and so on.

Procedure: preoperative learning

Within each trial the contingencies were as follows. Following an intertrial interval during which any response to the screen reset the interval, a positive pattern appeared on the screen together with some negative patterns. If the monkey touched any negative pattern the screen blanked, no food reward was dispensed, and the next trial in the task was presented after an intertrial interval of 20 s. If the monkey touched the positive pattern a food reward was dispensed. Simultaneously with the activation of the food dispenser the negative patterns all disappeared while the positive pattern stayed on the screen for 1 s, and the next trial in the task was presented after an intertrial interval of 10 s.

The animals were trained to criterion preoperatively. In each daily session trials continued until 100 correct responses had been accumulated. The last correct response was rewarded with the large food reward and all the preceding correct responses were rewarded with the small food reward. Each animal began by learning to choose the 30 positive patterns when each was presented with only one of its 14 negative patterns (see Stimulus material section), the same negative on all trials with that positive. Training continued in daily sessions in this stage until the animal made the required 100 correct responses in a total of 111 trials or fewer, i.e. made

90% correct choices in a session. In the subsequent stage of training there were two negative patterns on each trial, the first that had already been trained plus a new second negative pattern. In subsequent stages the number of negative patterns was increased to four, then seven, and finally 14. At each of these stages of training the animals continued training until the choices in a session were 90% correct.

Procedure: postoperative learning

In each daily session every trial presented five patterns, one positive and four negative. There were 30 possible individual positive patterns, each with its associated set of four unique negative patterns which were the same on every trial with that positive pattern. The positive patterns were those that had been trained preoperatively and the negative patterns were the first four that had been learned in preoperative training. The session continued until a certain total of correct responses had been accumulated, usually 15 or 30 correct responses. The within-trial contingencies were the same as in preoperative training. Training continued until the animal chose at 90% correct on average over a total of 120 correct responses. However, since it became clear that some animals were unlikely to reach this criterion, postoperative training was abandoned and an animal was scored as having failed to reach criterion if either >120 errors or >500 trials were accumulated in postoperative testing without reaching criterion.

Results

The animals took, on average, 3220 trials to complete the preoperative training schedule, during which they made on average 722 errors. The surgical groups into which the animals were assigned did not differ significantly in either trials or errors preoperatively ($F < 1$ in each case).

Figure 4 shows the main behavioural results. In postoperative testing, the monkeys had to search for a positive stimulus among five stimuli arranged in a left-to-right row. An error was committed if the monkey chose one of the four negative stimuli. Errors were classified according to the spatial position of the negative stimulus that was wrongly chosen, i.e. the response position of the error. This could be in any one of the five possible locations in the row. In Fig. 4, the response positions of errors are labelled with respect to the side of the lesion. For example, in the case of an animal with a right-hemisphere lesion the leftmost of the five possible response positions is most contralateral to the lesion ('Contra' in the horizontal axis of the left panel of Fig. 4) and the rightmost response position is most ipsilateral to the lesion ('Ipsi' in the same axis). In the left panel of Fig. 4 it can be seen that the group with unilateral optic tract section plus forebrain commissurotomy (Group OT+FC) made many errors in the positions that were ipsilateral to the optic tract section. Equally, the group with parietal leucotomy (Group PL) also directed many errors

Table 1 *Trials to criterion, total errors, and errors ipsilateral to the lesion*

Monkey	Trials to criterion	Total errors	Errors ipsilateral to lesion
Group PP			
S1 R	51	29	7
S2 R	75	28	6
S3 L	38	16	5
Mean	54.7	24.3	6
Group PP+FE			
S1 R	40	20	7
S2 R	73	25	2
S3 L	0	14	5
Mean	37.7	19.7	4.7
Group OT			
S4 R	156	44	14
S5 R	45	25	4
S6 L	42	20	12
Mean	81	29.7	10
Group FC			
S7 R	232	63	13
S8 L	78	31	5
S9 L	0	8	3
Mean	103.3	34	7
Group OT+FC			
S4 R	555 (F)	121	33
S5 R	249	126	50
S6 L	544 (F)	94	35
S7 R	330	102	26
S8 L	218 (F)	128	74
S9 L	190 (F)	146	119
Mean	347.7	119.5	56.2
Group PL			
S10 L	477 (F)	126	53
S11 L	112	67	30
S12 L	156	78	57
Mean	248.3	90.3	46.7
Group FL+FC			
S13 L	309	77	24
S14 L	96	28	9
S15 L	60	46	33
Mean	155	83	22

(F) = failed to reach criterion; R = operation on on the right; L = operation on on the left.

towards the side of their ablation. A weaker effect was seen, on average, in the group with forebrain commissurotomy combined with frontal lobectomy (Group FL+FC), and the remaining groups made few errors.

The right panel of Fig. 4 presents results from individual monkeys. As an index of the severity of neglect, the right panel shows the total of errors committed to the most ipsilateral response position for each animal (thus, the group means in the bars of the right panel correspond to the rightmost points in the left panel of Fig. 4). Analysis of variance of the data in the right panel of Fig. 1 confirmed that there were significant differences between groups [$F(6,17) = 4.51$, $P < 0.01$]. The group with optic tract section alone (Group OT) was taken as a benchmark (*see* Introduction) against which other groups were compared in a series of two-tailed designed comparisons. Group OT+FC

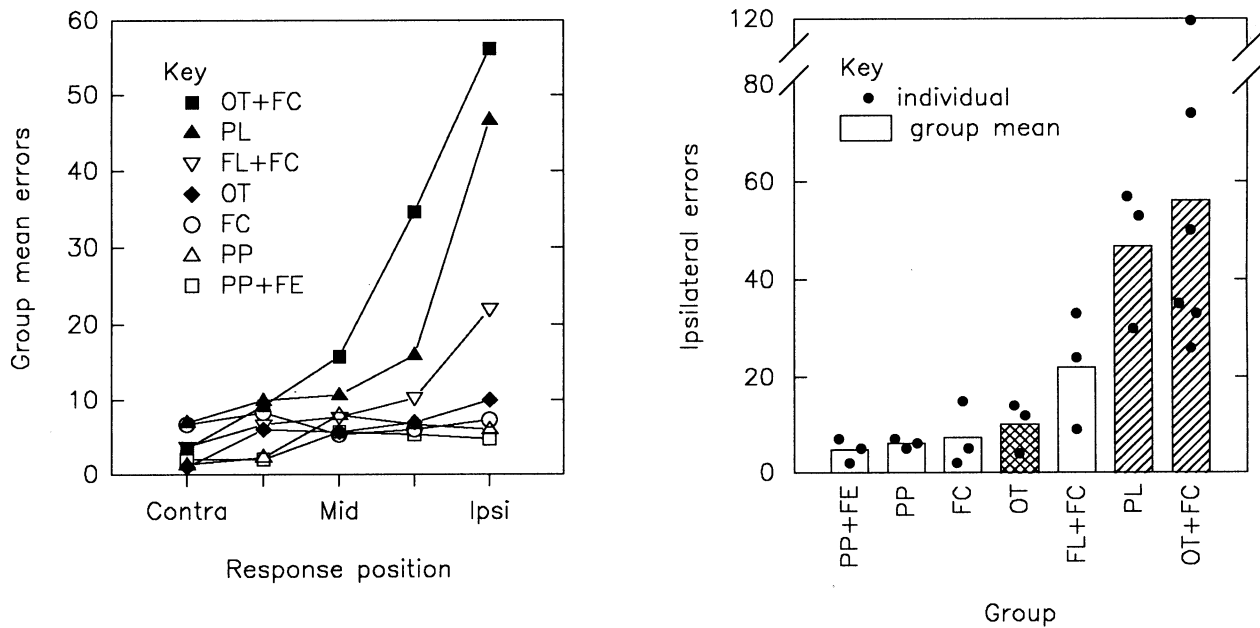


Fig. 4 Postoperative behavioural results. The *left panel* shows the group mean errors for each group of monkeys in a visual search task. The errors are classified by the position to which the error was directed, which could be to one of five positions ranging from the position ipsilateral to the animal's ablation (Ipsi) through the central position (Mid) to the position contralateral to the animal's ablation (Contra). The *right panel* shows group means in the total errors made to the position most ipsilateral to the lesion together with the corresponding results from individual monkeys; in the right panel, the bars show group means and each dot is one monkey. PP+FE = posterior parietal plus frontal eye-field ablation; PP = posterior parietal cortex ablation; FC = forebrain commissurotomy; OT = optic tract section; FL+FC = frontal lobectomy plus forebrain commissurotomy; PL = parietal leucotomy; OT+FC = optic tract section plus forebrain commissurotomy.

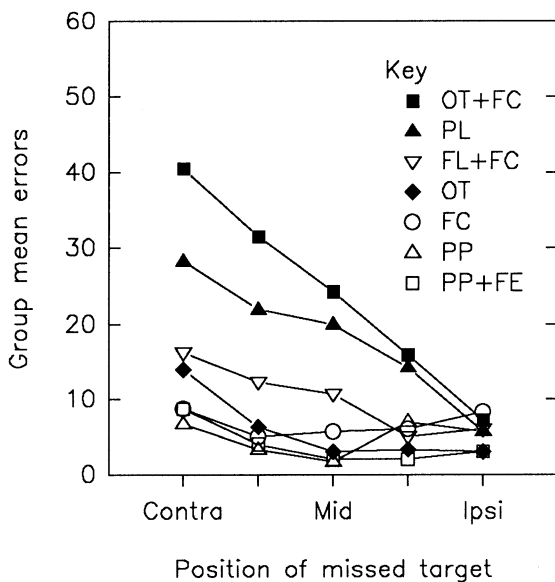


Fig. 5 Further analysis of the postoperative behavioural results. The errors are classified according to the spatial position of the positive, rewarded stimulus (the target) which the monkey should have chosen. See the legend to Fig. 4 for further details.

made significantly more ipsilateral errors than group OT [$t(17) = 3.21$, $P < 0.01$] as did also Group PL [$t(17) = 2.21$, $P < 0.05$]. The remaining groups were not significantly different from Group OT in their rate of ipsilateral errors ($t < 1$ in each case).

Figure 5 shows the errors analysed according to the spatial position of the missed target. For each trial on which a monkey chose one of the four negative stimuli, the error was here classified not by the spatial position of the erroneous response (as was done in Fig. 4) but by the spatial position of the positive stimulus which the monkey should have chosen on that trial. The monkeys in the groups with neglect tended to miss targets that were contralateral to the lesion.

Table 1 presents the results from individual animals in more detail. Trials to criterion for each animal is the total number of postoperative trials before the animal's performance reached a criterion of 90% correct responses, at which point testing ceased. Some of the animals failed to reach criterion within the limit of testing (>500 trials or >120 errors), and this is represented by '(F)' in the 'Trials to criterion' column in Table 1, which shows the total of postoperative trials in the case of animals which failed to reach criterion. The second column in Table 1 shows the total of errors committed by each animal in postoperative testing. The third column in the table presents the total of ipsilateral errors committed by each individual animal, which is also shown graphically in the right panel of Fig. 4. As expected, the groups which showed severe neglect in terms of ipsilateral errors also tended to show greater totals of errors and trials, and to contain animals that failed to reach criterion. Table 1 also shows whether the unilateral lesion was on the left (L) or right (R) for each subject. It can be seen that this factor appeared to have little effect on the

results. In Group OT+FC the animals with left optic tract section made more ipsilateral errors on average than the animals with right optic tract section, but this difference was not consistent across the individual animals.

Discussion

Substantial visual neglect was caused by unilateral visual disconnection, that is the combination of unilateral optic tract section with forebrain commissurotomy. The animals with visual disconnection showed a much more severe tendency towards lateralized errors (Figs 4 and 5) than animals with simple hemianopia, that is optic tract section alone. These findings establish quantitatively, by the comparison with the effects of hemianopia alone, that visual neglect can be produced experimentally in the monkey. The fact that neglect is caused by unilateral visual disconnection supports the representational account of visual neglect (Hornak, 1995). According to this account, the fact that neglect is not caused by optic tract section alone is explained by the ability of the blind hemisphere to construct and retrieve a memory-based representation of the visual world that is contralateral to the current point of fixation. This visual representation, in the hemisphere with optic tract section alone, is based on memories of visual information which arrived from the ipsilateral visual field in previous fixations that were directed contralateral to the current fixation point, and at least one important retrieval cue which can select the correct visual memories for retrieval is the visual information that is currently arriving in the ipsilateral hemifield. Neglect does follow, however, when unilateral optic tract section is combined with forebrain commissurotomy, even though the cortex is intact, because then the blind hemisphere is not only deprived of information arriving from the contralateral field but is also cut off from information arriving from the ipsilateral visual field, and therefore cannot build or retrieve a memory-based representation of the currently contralateral visible world. The implication of these findings is that in the normal animal each hemisphere maintains a representation of the contralateral visual world that is based both on perception (the analysis of current retinal input) and on memory (the retrieval of representations constructed from earlier retinal input).

Some important studies have investigated retrieval of spatially organized remote memories in neglect patients (Bisiach *et al.*, 1979, 1981; Meador *et al.*, 1987). For example, when a neglect patient was asked to describe from memory the street in which his home was situated, one side or the other of the street was omitted from the description, depending on the direction in which the patient imagined himself to be facing (Meador *et al.*, 1987). In such instances, the current retinal input at the time of memory retrieval is entirely irrelevant to memory performance, and the side of neglect is determined by a virtual direction of gaze in the remembered scene. However, neglect within the retrieval of scenes from remote memory may be functionally identical to neglect

within the current scene. Representation of the current scene is necessarily based partially on memory, for example, in the representation of scene features which are not within the current visual field, and retrieval from remote memory could simply be the limiting case where the representation is based on memory not partially but entirely.

The animals with cortical ablations in the posterior parietal cortex and frontal eye-field showed no more severe tendency towards lateralized errors than those with optic tract section alone (Fig. 4). As argued in the Introduction, the effect of simple hemianopia (optic tract section alone) can be used as a benchmark to gauge the severity of visual neglect in an experimental model, and to compare it with the severity of human visual neglect, since it is well established clinically that visual neglect is not simply a consequence of hemianopia. The present results therefore demonstrate quantitatively that cortical ablations in the posterior parietal cortex and frontal eye-field in the monkey do not produce a visual neglect that is analogous to human visual neglect. Unilateral ablations in these cortical areas do produce measurable behavioural effects, such as a change in the order in which food items are retrieved from a spatially distributed array by the monkey (Deuel and Farrar, 1993), but these changes have been described intuitively as less severe than human visual neglect by the many previous authors who have studied the effects of these cortical ablations in the monkey, as reviewed in the Introduction. The present results support such a judgement, and they further indicate that the adequacy of any putative monkey model of human visual neglect can, in future, be assessed quantitatively, by comparing it with peripheral hemianopia, rather than intuitively. The parietal cortex has important functions in visuospatial memory and visual shape discrimination, as recent ablation experiments in the monkey have shown (Latto, 1986; Traverse and Latto, 1986; Eacott and Gaffan, 1991; Gaffan and Harrison, 1993; Barrow and Latto, 1996), but the study of these important parietal functions may be hindered if the clinical features of visual neglect are falsely believed to reflect only parietal malfunction.

Unilateral frontal lobectomy combined with forebrain commissurotomy also failed to produce severe neglect (Fig. 4). The negative results from cortical ablations in the present study, both in the frontal lobectomy group and in the group with ablations in the posterior parietal area and frontal eye-field, imply that some other cortical areas, other than the frontal lobe and the posterior parietal area, are involved in the maintenance of the cortical representation of the contralateral visual world. We cannot rule out the possibility that some restricted cortical ablation in a discrete area of cortex outside the areas ablated in our posterior parietal group and in our frontal lobectomy group might by itself produce neglect as severe as that which we observed after forebrain commissurotomy and optic tract section. In the absence of any positive evidence for such a possibility, however, it seems more likely that a representation of the contralateral visual world is distributed in a widespread

fashion throughout many areas of cortex. An ablation study by Nakamura and Mishkin (1986) supports this suggestion. Their experiment showed that monkeys were behaviourally blind if one hemisphere was made blind by optic tract section and forebrain commissurotomy while in the other hemisphere all the cortex outside the visual cortex was removed, even though the striate, prestriate and temporal visual cortex were all intact bilaterally. No single area of nonvisual cortex was responsible for this effect; if any one of three mutually exclusive regions of nonvisual cortex called the sensorimotor, limbic and polysensory regions was left intact in the hemisphere with an intact optic tract, the monkey was not blind. These results show that visual perception depends on the interaction of visual cortex with widespread areas of nonvisual cortex. It seems likely that if total ablations of nonvisual cortex, similar to those in Nakamura and Mishkin's (1986) study, were made unilaterally but with the contralateral optic tract and cortex intact, unilateral visual neglect would follow. Combining the evidence about neglect, from the present study, with the evidence about blindness from the study by Nakamura and Mishkin (1986), we suggest that the representation of the visual world contralateral to the current fixation point depends on widespread interaction of visual with nonvisual cortex, and that this dependence is equal whether the representation is based on analysis of the current retinal information, or on memory of previous retinal information. This suggestion is consistent with the integrated-competition hypothesis of visual attention (Duncan, 1997).

This conclusion may appear to be at variance with the clinical evidence which indicates that visual neglect can be produced by a focal lesion in the fundus of the intraparietal sulcus (Denny-Brown and Chambers, 1958; Mesulam, 1981). However, focal lesions produced by disease processes are not necessarily limited to the cortex, but may also involve underlying white matter. The white matter inferior to the fundus of the intraparietal sulcus carries many of the pathways by which the posterior, retinotopically organized parts of the visual cortex can interact with nonvisual information, whether by direct corticocortical projections or by subcortical interactions. For example, cortical outputs to the basal ganglia and superior colliculus may pass through this region. Thus, cutting this white matter (parietal leucotomy, Group PL in Fig. 4), disconnects widespread areas of posterior visual cortex from their inputs and outputs. The neglect seen following parietal leucotomy therefore does not suggest a discrete cortical focus for neglect, but instead supports the idea that neglect is caused by disconnection of widespread posterior cortical areas.

In the monkey, it appears that visual disconnection of either the right or the left hemisphere causes equally severe contralateral visual neglect (Table 1, Group OT+FC). In the human brain, however, right hemisphere lesions cause a more severe neglect than left hemisphere lesions (Chain *et al.*, 1979). We can only speculate as to the origin of this species difference, but clearly one possibility is that, in the human brain, the representation of contralateral space is less

dependent on purely visual information, and more reliant on verbally mediated representation, in the left hemisphere than in the right hemisphere.

In summary, we have shown that visual neglect can be produced experimentally in the monkey by unilateral visual disconnection. This neglect is quantitatively analogous to human visual neglect in that it is more severe than the effect of hemianopia. The fact that it can be produced by visual disconnection, with the cortex intact bilaterally, supports the representational view of neglect. Further, we have argued that the representation of the contralateral visual world depends on widespread interactions of visual cortex with nonvisual cortex, both when the representation depends on analysis of current visual input and when it depends on memory.

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