Dissociated perceptual-sensory and exploratory-motor neglect

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Abstract

A patient with a right sided parietal lobe infarction manifested left sided sensory extinction in the visual, auditory, and tactile modalities but had only mild exploratory-motor neglect. In contrast, another patient with a right frontal haemorrhage demonstrated only left sided exploratory-motor hemispatial neglect. Tasks that combined perceptual and exploratory features elicited varying degrees of neglect in each patient. These two cases with dissociated neglect behaviour lend further evidence for behavioural specialisation within components of a cortical network for directed attention: sensory-representational aspects mediated primarily by the parietal component, motor-exploratory primarily by the frontal component. These cases also highlight the need to include and distinguish among several different measures of neglect in the clinical investigation of patients with hemispatial inattention.

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Patients with left-sided hemispatial neglect associated with right-sided hemispheric lesions fail to attend to sensory stimuli and fail to explore objects within the left hemispace.[1-3] Different theories of neglect have emphasised defects in sensation and recognition (amorphosynthesis),[4] attention,[5] oculomotor control,[6] the internal representation of space,[7] arousal,[2 8] and the orienting response towards stimuli in the contralateral hemispace (directional hypokinesia).[9 10]

Mesulam's cortical network theory[11 12] highlights the relative behavioural specialisation of the parietal and frontal lobes and the cingulate gyrus in directed attention: the posterior parietal component provides an internal sensory map of extrapersonal space, the frontal component a mechanism for scanning and exploring, and the cingulate a spatial map for motivational relevance. The components are tightly interconnected, so damage to any one of them causes unilateral neglect which is usually multimodal and evident in a variety of behaviours.[2 11-13] In some instances, however, clinical symptoms may be dissociated on the basis of lesion site.[14]

Clinical tests for neglect include line-crossing, copying or drawing familiar objects such as a house or clock, visual target cancellation tasks, blindfolded manual exploration, line-bisection, and bilateral simultaneous stimulation using visual, auditory, and tactile stimuli. It has been common practice to consider the number of tests failed as an indication of the severity of neglect even though each test emphasises a different behavioural process.[15-18] For example, blind-folded manual exploration is a pure measure of exploratory-motor neglect while visual target cancellation and line-crossing also require perceptual-sensory processes. Thus two different tasks may elicit different degrees of neglect in the same patient.[3] Altering stimulus attributes within the same task may also affect the degree of neglect shown by the patient.[3 19-22]

We present further evidence for dissociated neglect in two patients: one with a parietal infarction and neglect on tasks primarily emphasising sensory-perceptual aspects and another with a frontal lesion and neglect only during tasks emphasising exploratory-motor features.

Case reports

Procedure Each patient had testing that attempted to isolate sensory and exploratory-motor components of neglect. For the measurement of exploratory-motor neglect, we investigated the *exploration* of ipsi- and contralesional space instead of motor neglect or limb hypokinesia, the underutilisation of an otherwise nonparetic limb.[23] Exploratory-motor neglect was tested by blindfolded manual exploration.[24] The patients were asked to detect by palpation a small target placed in front of them in 9 positions symmetrically each to their left and right (fig 1). Each target position was presented once (total trials = 18). The time to reach the target on each trial in each hemispace was recorded. Both patients were tested with their nonparetic right hand.

Sensory extinction was tested with bilateral simultaneous stimulation in the auditory, tactile and visual modalities. Visual exploration, combining perceptual-sensory and exploratory-motor aspects, was evaluated by giving the patients a target cancellation task with a random array of letters as stimuli and asking them to locate all the "As".[21] They were also provided with a sheet of paper on which were printed lines of single words, sentences and strings of "Xs" and were asked to read the words out loud. Clock and cube drawings were also obtained.

Comparisons were made with laboratory-based data for groups of age-matched control subjects for letter cancellation and manual exploration tasks.

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Figure 1 The blindfolded manual exploration task tested exploratory-motor neglect. The patient detected by palpation a small target located in 9 positions on the left and 9 symmetrically on the right. Times to reach the targets were recorded then averaged for each hemispace.

Patient 1 A previously healthy 72 year old right handed man was admitted to the Beth Israel Hospital when he experienced a sudden headache, left arm numbness and slurred speech. He had a left hemiparesis, left homonymous hemianopsia, and blunted awareness. Cranial CT scan revealed a right-sided middle cerebral artery infarction extending from the Sylvian fissure to the parietal region involving the optic radiations, angular gyrus, and supramarginal gyrus (fig 2).

Nine months later he was evaluated because of persistent cognitive and behavioural difficulties. Neurological examination revealed a mild left hemiparesis involving the arm more than the leg or face, a left homonymous inferior quadrantanopsia, and increased deep tendon reflexes on the left.

During neuropsychological examination he was alert, oriented, and cooperative. Mild irritability and anosognosia were noted. The most striking feature of the examination was left-sided unilateral inattention. On bilateral simultaneous stimulation, there was left-sided extinction on 6 of 6 trials in both the visual (within intact fields) and tactile modalities and on 5 of 6 trials in the auditory modality. In contrast, 12 trials (6 right, 6 left) of unilateral stimulation in each modality elicited no errors for either side.

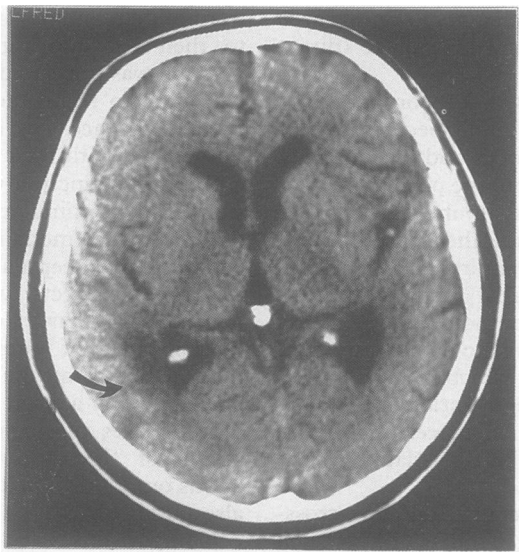

Figure 2 CT scan of the head in patient 1 demonstrating an acute infarction (arrow) of the right parietal lobe involving angular and supramarginal gyri and optic radiations.

On tasks which combine perceptual-sensory and exploratory-motor aspects of attention, deficits were less prominent. On the visual target cancellation task the patient located 29 of 30 targets on the right and 25 of 30 targets on the left (fig 3a). The number of omissions on the left was outside normal limits determined from a laboratory based age matched control group (eight normal control subjects, mean 67·38 years old, range 62–73 years, omitted a mean (SD) total of 1·38 (1·59), on the left and 0·88 (0·99) targets on the right). On the reading task he failed to read 20% of the 178 words; one-quarter of the ignored words were on the right side of the page (fig 4a). We have not established control values for the number of words omitted during the reading task since it is unlikely that normal individuals would ignore any words. The patient's spontaneous cube drawing was deficient but showed no signs of gross neglect. His spontaneous clock drawing had only mild misplacement of numbers on the left.

Manual exploration of space with the right hand, emphasising exploratory-motor aspects of neglect, was slow bilaterally but not significantly different across the left and right sides. Wilcoxin's signed rank test revealed no significant difference in the time to find the target in the 9 positions on the left and their mirror locations on the right. The average, mean (SD), time to reach the target was 7·56 (5·59) seconds on the right and 6·33 (7·23) seconds on the left, both exceeding normal limits (in eleven normal subjects, mean (SD) age 67·91 (4·72) years, the mean (SD) corresponding times to locate targets with the right hand was 5·23 (2·94) seconds in the left hemispace and 5·09 (3·29) seconds in the right). Thus this patient's best performance was observed on a pure measure of exploratory-motor neglect, worst performance on sensory extinction, and intermediate performance on tasks sensitive to both (table).

Patient 2 A 69 year old ambidextrous, hypertensive woman developed an acute myocardial infarction and was admitted to hospital locally and treated with tissue plasminogen activator (t-PA) and heparin. The next day she noticed sudden left arm weakness, and a head CT revealed a right-sided frontal haemorrhage believed to be related to the t-PA therapy.[25] The heparin was discontinued, and she was transferred to the Brigham and Women's Hospital one week later.

She was alert and acutely aware of her deficits. She had a right gaze preference and was unable to look voluntarily or reflexively past midline at objects to the left. However, she was aware of and able to describe objects to her left. Optokinetic nystagmus (OKN) was absent

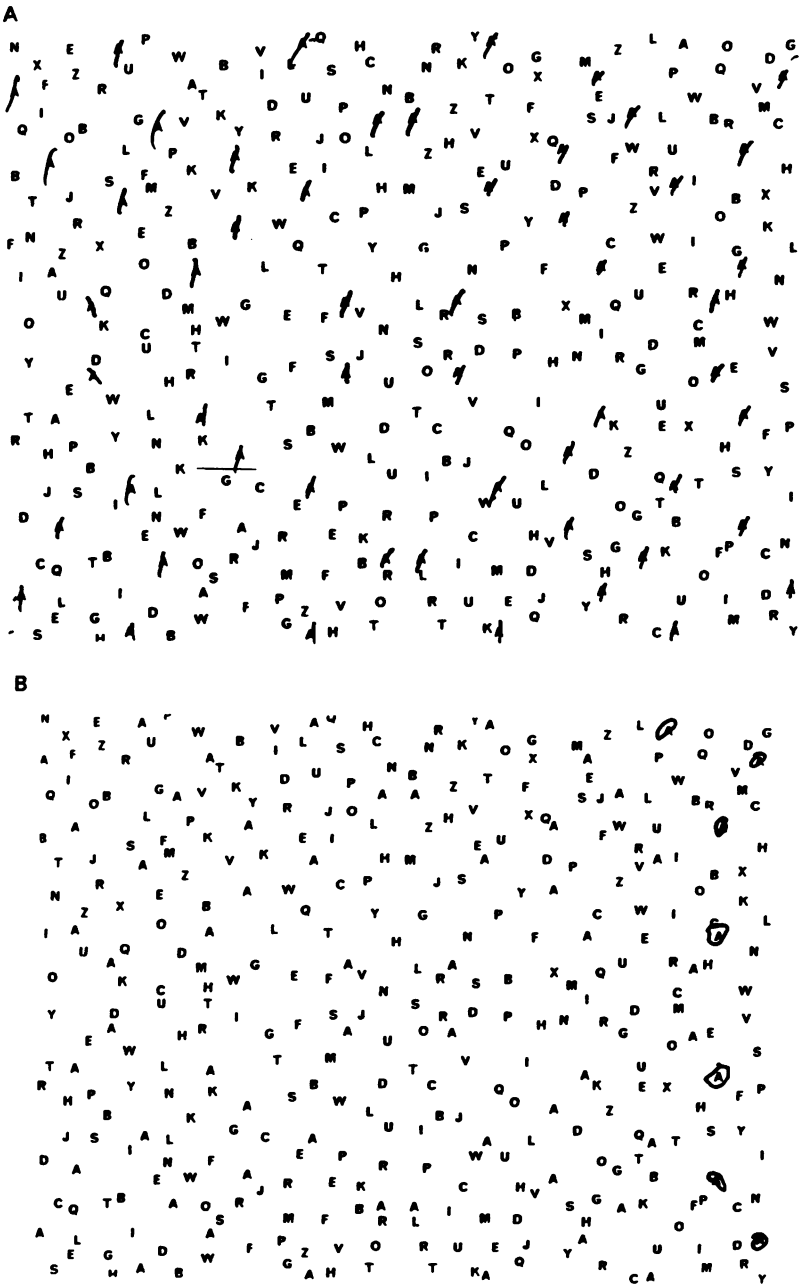

Figure 3 The patients were instructed to find the "A's" in the visual target cancellation task. Patient 1 (a) had a mild left-hemispatial neglect; patient 2 exhibited severe neglect behavior (b). See text for details.

with stimuli moving from the patient's left to right but normal in the opposite direction. With oculocephalic manoeuvres, her eye movements were smooth and full. There was very mild left face and leg weakness, but her left arm was plegic. The left triceps, biceps, and brachioradialis reflexes were hyperactive, but both plantar responses were flexor. Her visual fields were full to confrontation, and light touch, temperature, and proprioceptive modalities were normal.

There was no extinction to visual, tactile, or auditory bilateral simultaneous stimulation. However, she exhibited neglect on tasks including or exclusively addressed to exploratory-motor aspects. She drew a clock with the numbers only on the right. She copied a cube two-dimensionally. On the random letter cancellation test, using her unaffected right hand she began in the upper right hand corner of the test sheet and proceeded vertically, searching only the extreme right hand margin. When asked to identify the left hand margin of the paper, she did so promptly and accurately, but then resumed her search on the right (fig 3b).

MRI confirmed a right posterior frontal haemorrhage affecting the precentral gyrus, the frontal eye fields, and underlying subcortical white matter (fig 5). There was no significant mass effect.

Two weeks later her eye movements had improved significantly. Horizontal saccades were almost normal though she was unable to bury her sclera completely to the left. She still had mild difficulty tracking visual stimuli moving from her right to left. OKN was symmetrical. Exploratory-motor neglect, on the other hand, was still present. During the reading task she read all the words in the first four lines correctly, however she ignored all words to the left of midline after a series of "Xs" interrupted the sequence in the middle of the page (33% words missed out of the 178 total) (fig 4b). During the blindfolded manual exploration task, while using her right hand she was significantly slower detecting the target object in the left hemifield than in mirror locations on the right (Wilcoxin's $T = 1{\cdot}5$, $p < 0{\cdot}02$). The average, mean (SD), time to reach the target was 3·56 (1·01) seconds on the right side, which was within normal limits, but 13·67 (16·86) seconds on the left side, exceeding normal values [5·23 (2·94) seconds], (table).

Discussion

We describe two patients, one with a parietal lesion and the other with a frontal lesion, who demonstrated dissociated neglect behaviour. In patient 1 the homonymous inferior quadrantanopsia localised the lesion to the right parietal lobe[26] although the left hemiparesis and hyperreflexia indicated involvement of descending motor fibres as well. His neglect was worst during perceptual-sensory tasks. In contrast patient 2 demonstrated neglect most noticeably during exploratory-motor tasks, and her haemorrhage primarily affected right frontal lobe structures. The plegic left hand implies involvement of the motor cortex, and the supranuclear paresis of horizontal leftward gaze implicates extension of the lesion anteriorly into the frontal eye fields.[27] The asymmetrical OKN suggests the haemorrhage or oedema may have initally extended into deep white matter tracts within the parietal lobe,[28] yet on subsequent examination the OKN was normal, and the patient continued to demonstrate neglect. Radiological studies confirmed the lesion site in both cases.

Neglect of left hemispace from a posterior right-sided parietal lesion as in patient 1 is a well-established observation.[29] Several authors have also already reported left-sided neglect from a right frontal lesion, similar to that in patient 2, both in humans[30 33] and in animals

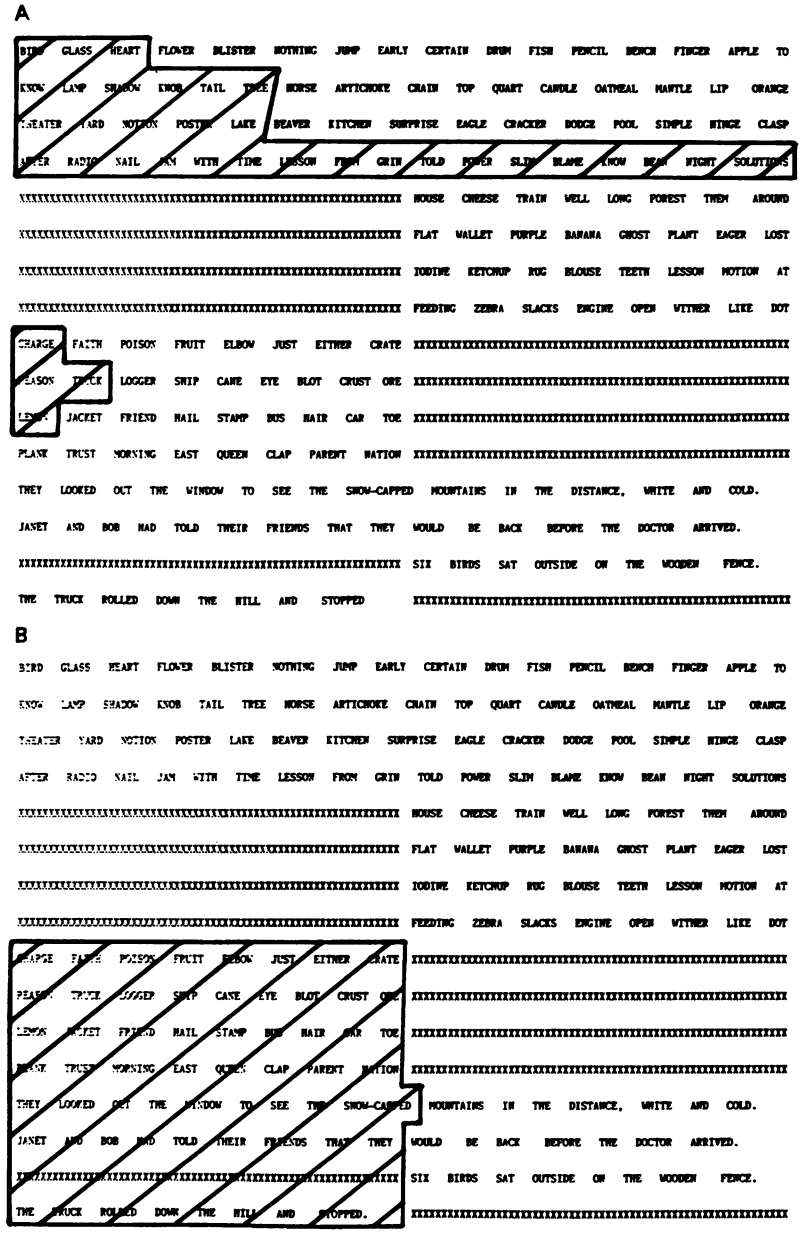

Figure 4 During the reading task the patients were asked to read all the words aloud. The hatched areas indicate the words ignored by patient 1 (a) and patient 2 (b); each demonstrated varying degrees of left-sided neglect. See text for details.

Table 1 Performance on tests of neglect. *

Lesion Site	*Patient 1 Right parietal lobe*	*Patient 2 Right frontal lobe*
Left-sided Extinction during Bilateral Simultaneous Stimulation		
Visual	6/6 trials	absent#
Tactile	6/6	absent#
Auditory	5/6	absent#
Visual Target Cancellation		
Omissions on Left	5	30
Omissions on Right	1	23
Reading Task		
Words omitted on Left (% of total)	15%	34%
Words omitted on Right (% of total)	5%	0
Manual Exploration		
Mean Target Detection Time on Left	6·33 seconds	13·67
Mean Target Detection Time on Right	7·56	3·56

*See text and figures for descriptions of tests. Bilateral simultaneous stimulation emphasizes perceptual-sensory features of neglect, while manual exploration highlights the exploratory-motor aspects. The visual target cancellation and reading task are sensitive to both.
#Bilateral simultaneous stimulation in patient 2 was tested multiple times at the bedside but not with a systematic series of trials as in patient 1.

with experimental injury of prearcuate area 8, the frontal eye fields.[34 39] Our two cases, however, are of special interest because they demonstrate dissociated neglect for sensory and exploratory-motor tasks in a manner consistent with the model of attention which separates these behavioural components.[11 12]

In patient 1 sensory extinction might have been a result of a disrupted parietal sensory map; motor responses were relatively unaffected. Patient 2's neglect was most obvious during the letter cancellation and blindfolded search tasks. Her prompt identification of the left-sided edge of the test sheet when instructed to do so during letter cancellation suggested she was aware of left hemispace but either unmotivated or incapable of spontaneously exploring it. Exploratory-motor neglect following a frontal lesion could therefore be attributed to a disordered mechanism for the planning and execution of motor acts in the left hemispace.[10–12]

Our cases complement previous demonstrations of dissociated parietal and frontal neglect in animals and humans. In monkeys with ablation of the inferior parietal lobule, Heilman *et al*[40] observed extinction of visual, tactile and auditory stimuli during bilateral simultaneous stimulation without abnormalities in eye movements or placing responses. Watson *et al*[41] demonstrated that monkeys with frontal arcuate gyrus lesions may have an intentional defect and not react to contralateral stimuli, independent of any perceptual abnormalities. The patient described by Daffner *et al*[14] had dissociated exploratory-motor and perceptual-sensory neglect from sequential strokes to the right frontal and posterior parietal lobes.

The performance of our two patients also highlights the multimodal and multifactorial nature of tests of neglect. Many of the tests, such as letter cancellation, copying a figure, reading or line-crossing, fail to isolate sensory and exploratory behavioural components and require both intact visual perception and eye or limb movement. A clock with numbers drawn only on the right could reflect either a disinclination to draw them on the left or an impaired awareness of the left side of the clock. Many recent authors have studied patients[13 33 42–45] and animals[45] with neglect and attempted to separate the sensory and exploratory factors. At present, the only "pure" tests of sensory neglect are bilateral simultaneous stimulation and Posner's paradigm for testing covert attention,[47] and the most direct test of exploratory-motor neglect is the blindfolded tactile search task. Currently no formal paradigm appropriate for human subjects adequately isolates the limbic or motivational aspects of neglect.[3] Future investigations of neglect may benefit from designing tasks that isolate these features.

Most patients with unilateral neglect will still have multifactorial deficiencies because the network for directed attention is so heavily interconnected. Occasionally, however, as in our two patients, the neglect is dissociated in a way which supports behavioural specialisation within the cortical network for directed attention.

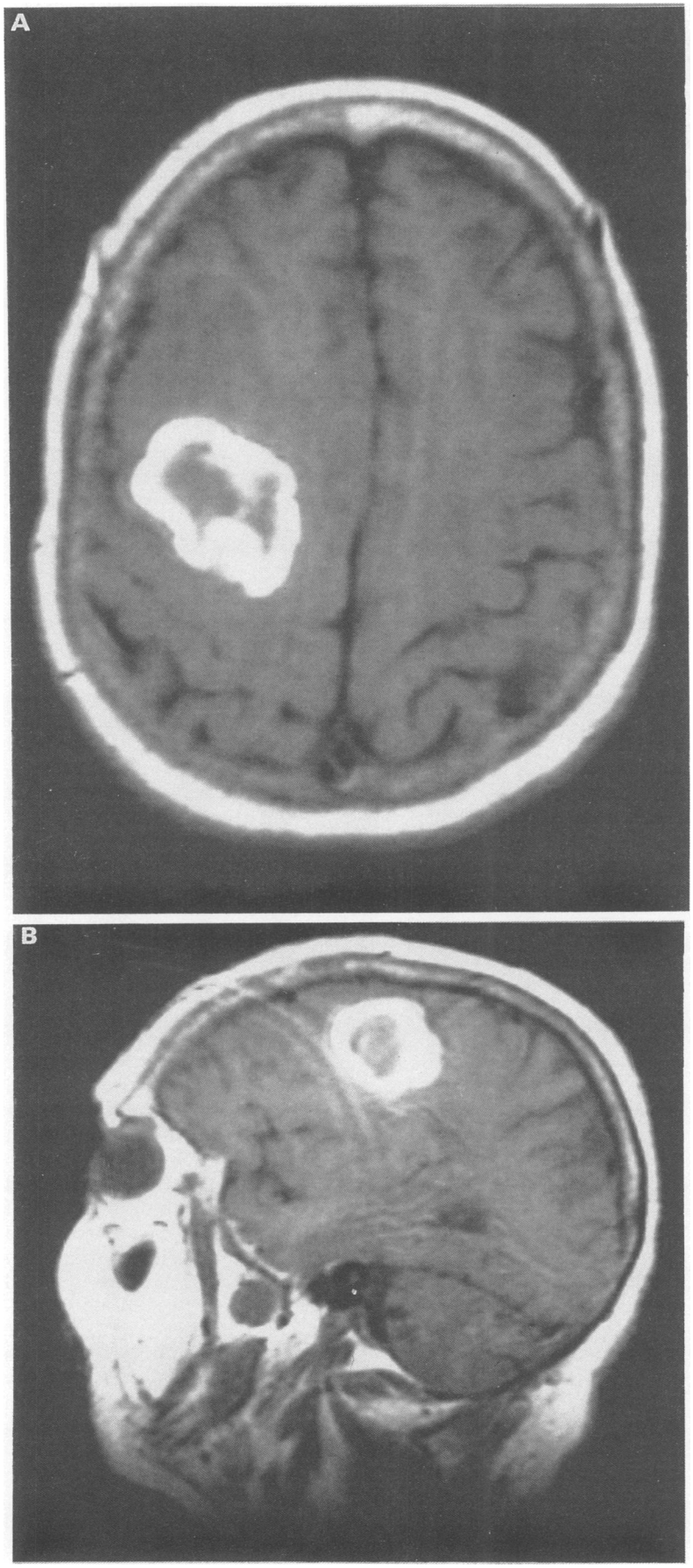

Figure 5 Patient 2. MRI in the axial (a) and sagittal (b) planes demonstrating a 10 day old haemorrhage in the right posterior frontal lobe involving motor cortex, frontal eye fields, and subcortical white matter.

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