

Visual neglect after right posterior cerebral artery infarction

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Objectives: To investigate the characteristics and neuroanatomical correlates of visual neglect after right-sided posterior cerebral artery (PCA) infarction.

Methods: 15 patients with acute PCA strokes were screened for the presence of neglect on a comprehensive battery of cognitive tests. Extra tests of visual perception were also carried out on six patients. To establish which areas were critically associated with neglect, the lesions of patients with and without neglect were compared.

Results: Neglect of varying severity was documented in 8 patients. In addition, higher-order visual perception was impaired in 5 of the 6 patients. Neglect was critically associated with damage to an area of white matter in the occipital lobe corresponding to a white matter tract connecting the parahippocampal gyrus with the angular gyrus of the parietal lobe. Lesions of the thalamus or splenium of the corpus callosum did not appear necessary or sufficient to cause neglect, but may mediate its severity in these patients.

Conclusions: PCA stroke can result in visual neglect. Interruption of the white matter fibres connecting the parahippocampal gyrus to the angular gyrus may be important in determining whether a patient will manifest neglect.

Visual neglect is a frequently observed syndrome after unilateral brain damage, characterised by a failure to respond to contralesional stimuli.^{1–2} Neglect is particularly prevalent acutely after right-hemisphere stroke. Most patients with the syndrome have damage in the territory of the middle cerebral artery, although the critical lesion areas responsible for causing neglect are controversial.^{2–5} Neglect has also been reported after lesions of the thalamus,^{2–6–7} but it is less well documented that the syndrome can follow strokes in the wider territory of the superficial posterior cerebral artery (PCA).

The anatomy of neglect after PCA infarction was first directly addressed only recently by Mort *et al.*⁵ Visual neglect was associated with lesions that extended from the occipital lobe anteriorly to the parahippocampal region and centred on an area of white matter in the ventromedial temporal lobe. The authors raised the possibility that disruption of the parietotemporal white matter tracts may explain the presence of neglect in these patients. Interestingly, in this context, a recent study⁸ using diffusion-weighted imaging and probabilistic tractography in healthy humans has documented robust projections between the parahippocampal gyrus and the angular gyrus of the parietal lobe, homologous to the tract that connects the same regions in non-human primates.⁹ A second study by Park *et al.*¹⁰ reported several areas as being associated with visual neglect, including the parahippocampal gyrus and the thalamus. However, multiple regression analyses showed that the only combination of lesions to contribute considerably to the frequency and severity of neglect was damage to both the occipital lobe and the splenium of the corpus callosum. The authors proposed

that this pattern of damage results in deafferentation and disconnection of visual information to one hemisphere, which may be sufficient to cause neglect.

In addition to neglect, PCA infarction may also lead to other visual perceptual deficits, as might be expected with damage to areas characterised as being in the ventral visual pathway.¹¹ However, visual perceptual deficits from damage to areas in the ventral visual stream in the right hemisphere are usually documented only in the context of category-specific agnosias, such as prosopagnosia or landmark agnosia (or topographagnosia).^{12–16} It therefore remains an open question whether damage to the ventral medial temporal and occipital cortices results in more general perceptual impairments. We aimed (1) to examine the characteristics of neglect and perceptual deficits from PCA infarction, by assessing patients with right-sided PCA infarction on a battery of neglect tests and a subgroup on tests of visual perception; (2) to investigate which anatomical areas are most commonly damaged in PCA neglect, paying particular attention to those areas implicated in previous studies (the thalamus, parahippocampal gyrus and splenium); and (3) to explore whether disconnection of cortical areas is a likely cause of neglect after PCA infarction.

METHODS

Participants

Fifteen patients were recruited for this study and all gave informed consent to participate, according to the Declaration

Abbreviations: DTI, diffusion tensor imaging; PCA, posterior cerebral artery

Table 1 Patient details and performance on the neglect battery

ID	N1	N2	N3	N4	N5	N6	N7	N8	C1	C2	C3	C4	C5	C6	C7
Imaging protocol	CT	MRI	CT	CT	CT	CT	MRI	MRI	CT	CT	CT	MRI	CT	MRI	MRI
Age (years), sex	75, M	95, M	61, M	66, M	71, M	77, F	75, F	67, F	77, F	63, F	74, F	83, F	67, M	59, F	63, F
Interval (days)*	10	2	9	6	8	25	4	15	0	4	11	31	5	7	8
Constructional apraxia†	Yes	Yes	Yes	Yes	No	NT	Yes	Yes	NT	NT	No	Yes	NT	Yes	No
Visual field deficit	LH	LH‡	LH	LH	LH	LH	LH	LSQ	LH	LSQ	LIQ	LH‡	LH	LH	LH
Lesion volume (cm ³)	67.3	13.6	56.2	44.7	21.7	52.6	5.9	29.4	11.5	31.0	25.0	6.4	10.5	6.1	7.1
Neglect battery															
Line bisection (cm)§	7.5	6.5	1.7	3.5	1.3	-6.2	0.4	-0.5	-0.6	-0.4	-1	-0.7	-1.6	-0.8	0
L (Mes)/30	0	0	NT	7	25	0	1	22	26	NA	26	NT	30	29	29
R (Mes)/30	2	2	NT	17	28	11	22	25	25	NA	28	NT	30	28	29
Total (Mes)/60	2	2	NT	24	53	11	23	47	51	NA	54	NT	60	57	58
L (BIT)/27	0	0	4	19	19	13	0	26	26	25	27	26	27	26	27
R (BIT)/27	10	7	15	20	25	14	23	25	25	24	27	24	27	25	27
Total (BIT)/24	10	7	19	39	44	27	23	51	51	49	54	50	54	51	54
Copying shapes	NA	Fail	Fail	Fail	Fail	NT	NA	Pass	Pass	NT	Pass	Pass	Pass	Pass	Pass
Reporting objects	NT	Fail	Fail	Pass	Pass	Fail	NT	Pass	Pass	NT	Pass	Pass	Pass	Pass	Pass
Comb test	Fail	Pass	Pass	Pass	Pass	NT	Pass	Pass	Pass	NT	NT	Pass	Pass	Pass	Pass
Razor test	Fail	Fail	Pass	Pass	Pass	NT	Pass	Pass	Pass	NT	NT	Pass	Pass	Pass	Pass
Drawing	Fail	Fail	Fail	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass	Pass

BIT, behavioural inattention test; CT, computed tomography; Fail, evidence of neglect; LH, left hemianopia; LSQ, left superior quadrantanopia; Mes, Mesulam's shape cancellation test; MRI, magnetic resonance imaging; NA, patient unable to compete test; NT, not tested; Pass, no evidence of neglect.

*Interval between stroke and assessment.

†As tested by the ability to draw a copy of a three-dimensional cube.

‡Initially an apparent hemianopia, which resolved to an upper quadrantanopia.

§Mean rightward deviation.

of Helsinki. The study was approved by the relevant hospital research ethics committees. All patients were right-handed and had been admitted to hospital with acute right-hemisphere stroke, subsequently confirmed to involve infarction in the territory of the PCA. They were assessed within 31 days of stroke (mean (standard deviation (SD)) interval between stroke and assessment 9.7 (8.4) days). Visual fields were assessed clinically using a confrontation technique (table 1).

Cognitive assessment Neglect battery

A comprehensive battery of tests was carried out to assess various aspects of neglect, including "peripersonal", "extrapersonal" and "personal" neglect. Full details of the battery are available as supplementary materials online at <http://www.jnnp.bmjournals.com/supplemental>.

Additional tests of visual perception

Six patients were administered a selection of tests of visual perception. These tests were chosen to encompass aspects of visual processing from the basic level (figure-ground segregation) to complex visual identification (recognition of visually degraded objects). Full details of the additional tests are available as supplementary materials online at <http://jnnp.bmjournals.com/supplemental>.

Anatomical assessment

Brain lesions were imaged by computed tomography or magnetic resonance imaging and plotted using MRICro software (Chris Rorden, Columbia, SC, USA. www.mricro.com) using a graphics tablet (Wacom Intuos A6 Wacom Technology Corporation Vancouver, WA, USA). A T1-weighted

template consisting of 12 axial slices was used to demarcate the lesions for all patients. Lesion volumes were computed using MRICro software tools. MRICro was also used to analyse the degree of overlap of lesions in the two patient groups and to make comparisons between them.

RESULTS

Results of cognitive tests Neglect battery

Table 1 shows the performance of the patients on the battery of tests. The patients were split into two groups according to whether or not (controls) they showed any evidence of neglect (patients N1–N8 and patients C1–C7, respectively). No significant differences were found between the two groups in terms of age ($p>0.1$) or interval between stroke and assessment ($p>0.1$).

The range of severity of neglect was large. For example, N1 and N2 presented with clear evidence of neglect on almost all of the tests. On the other hand, N8 passed all the neglect tests except Mesulam's shape cancellation task, on which the patient was mildly impaired. Nevertheless, N8 invariably started from the right side and worked leftwards when performing the tests, which has been considered to be a sensitive marker for neglect.¹⁷

All the patients (N1–N8) showed evidence of visual neglect for peripersonal space, failing at least in one of the cancellation tasks. On the line bisection test, five patients (N1–N5) showed a clear rightward deviation. However, N6 showed a very large leftward deviation, a phenomenon which has been documented in patients with acute hemianopia.¹⁸ Personal neglect was rare, with only two patients failing the razor test (N1 and N2) and only one of these also failing the

Table 2 Performance on the tests of visual perception

ID	N2	N3	N4	N5	N8	C2
Interval (days)*	44.00	14.00	196.00	19.00	60.00	22.00
Shape detection	19/20 (pass)	NT	NT	20/20 (pass)	20/20 (pass)	20/20 (pass)
Fragmented letters	7/20 (<5 centile)	2/20 (<5 centile)	15/20 (<5 centile)	10/20 (<5 centile)	18/20 (pass)	20/20 (pass)
Silhouettes	4/30 (<5 centile)	14/30 (<5 centile)	9/30 (<5 centile)	12/30 (<5 centile)	8/30 (<5 centile)	16/30 (5–10 centile)

NT, not tested; pass, no evidence of neglect.

*Interval between stroke and assessment.

comb test (N1). Finally, three patients (N1–N3) were impaired at drawing objects from memory, which may reflect an impairment of visual representation.

Visual perceptual tests

Table 2 shows the results of the three visual perceptual tests. None of the patients failed the shape detection test, indicating that they had no impairment of early visual processing abilities. Nevertheless, N2–N5 were impaired on a relatively easy test of visual form perception—the fragmented letters test from the visual object and space perception. The same patients, and patient C4, were impaired on the Silhouettes test from the visual object and space perception, a more stringent test of visual object perception. N8 passed the Silhouettes test, although the score fell below the 10th centile for N8's age group.

Anatomical data

Figures showing the extent of the lesions in each patient are available as supplementary materials online at <http://www.jnnp.bmjournals.com>. Neglect was generally associated with larger lesions and there was a significant difference between the lesion volumes of N1–N8 and C1–C7 (mean (SD) of N1–N8 36.4 (22.0) cm³; C1–C7 13.9 (10.0) cm³, $t = 2.5$, $df = 13$, $p < 0.05$). Six patients (N1–N4, N6 and N8) in the neglect group had lesions extending into the medial temporal lobe, involving the fusiform gyrus, lingual gyrus, parahippocampal gyrus and hippocampus. Another patient (N5) had a lesion that extended into the parietal lobe. Interestingly, N7's lesion was restricted to the

occipital lobe. Among the controls, the lesion extended anteriorly as far as the parahippocampal gyrus in only two patients (C1 and C3). Of these, only C3 had fairly extensive involvement of the parahippocampal gyrus. There was a degree of thalamic involvement in five of the patients with neglect (N1, N3, N4, N8) and, to a very limited extent, (N2) but in none of the controls. Also, half of the patients with neglect (N1–N4) had damage to the splenium, but neither patients N5–N8 nor any of the controls had any involvement of this area.

To determine which anatomical regions were most associated with neglect, we compared the lesions of the patients with neglect with those of the controls. In the patients with neglect, there was maximal overlap of lesions in the white matter of the occipital lobe and a high degree of overlap extending anteriorly into the ventral medial temporal lobe (fig 1A). In the controls, there was also an area of common damage in the occipital lobe close to the region most often damaged in the patients with neglect (fig 1B), reflecting the fact that both groups of patients have infarction in the same vascular territory. Figure 1C shows the key direct comparison between the two groups of patients. Importantly, this shows an area within the white matter of the occipital lobe, which is damaged in all the patients with neglect but in none of the controls.

In healthy humans, diffusion tensor imaging (DTI) has identified a white matter tract coursing from the parahippocampal gyrus to the angular gyrus.⁸ Both of these areas have been associated with visual neglect.⁵ Although we found no area of overlap close to the parahippocampal gyrus, it is

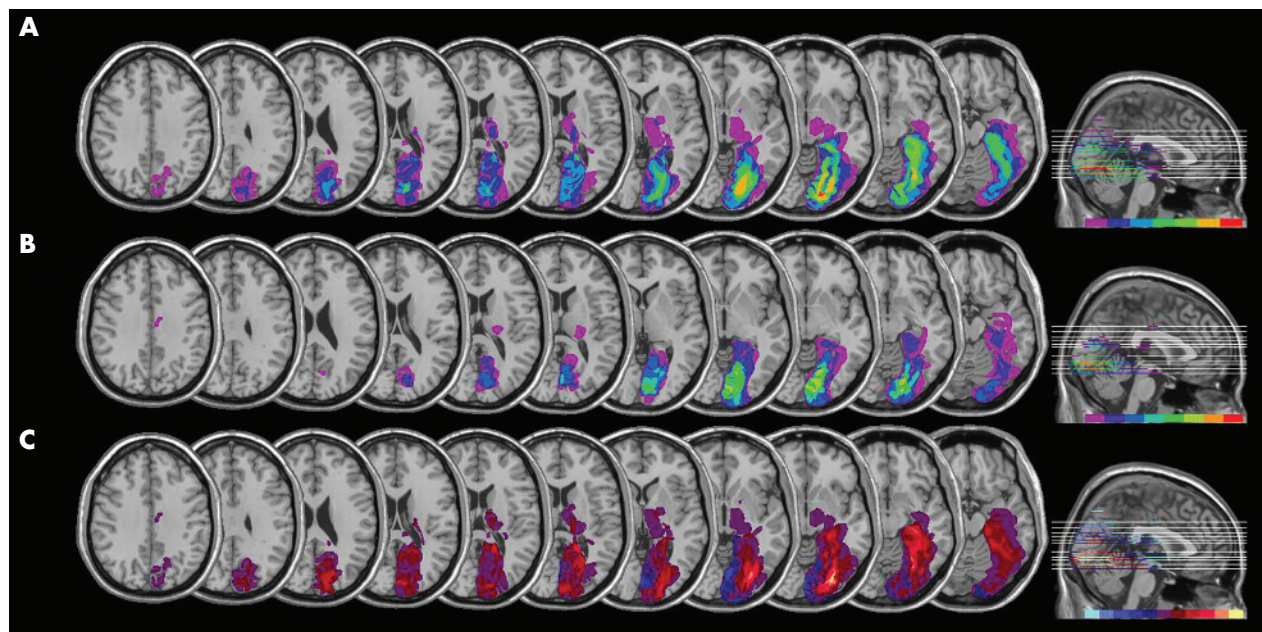


Figure 1 (A) Overlap of lesions of patients with neglect (N1–N8). (B) Overlap of controls (C1–C7). (C) Subtraction plot showing areas most associated with neglect (A,B).

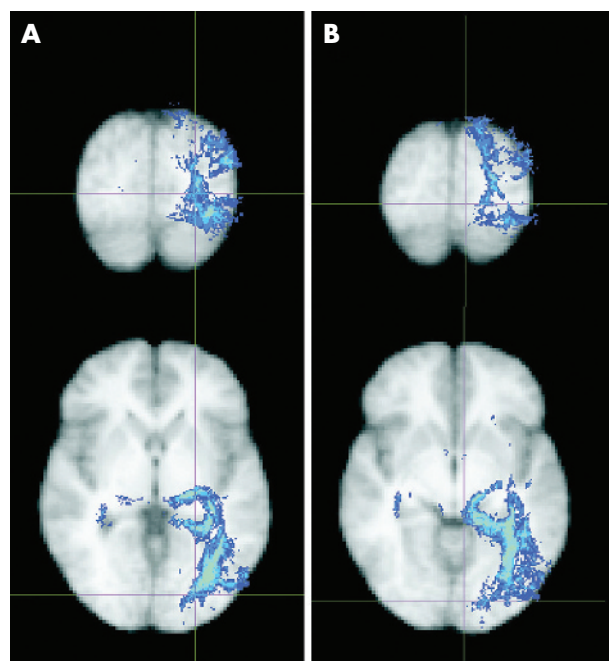


Figure 2 (A) Crosshairs indicate the centre of the area most associated with neglect in our study superimposed on diffusion tensor imaging (DTI) data from healthy adults showing the probabilistic white matter tract from the parahippocampal gyrus to the angular gyrus (inferior longitudinal fascicle). (B) Crosshairs indicate the area of maximal overlap in the controls superimposed on DTI data⁸ from healthy adults showing the probabilistic white matter tracts from the parahippocampal gyrus to the angular gyrus.

possible that lesions within the white matter of the occipital lobe disrupt the tract identified by Rushworth *et al.*⁸ Figure 2A shows the area maximally associated with neglect in our study, with the DTI data showing the probable course of the white matter tract from the parahippocampal gyrus to the angular gyrus⁸. The area of maximal lesion overlap lies within this tract, whereas the area most commonly damaged in the controls lies outside the tract (fig 2B).

DISCUSSION

Our study demonstrated visual neglect and visual perceptual impairments of varying severity after right-sided PCA stroke. It is important to note that the brain regions damaged in the patients with neglect in our study are quite distinct from the lateral parietal and frontal regions most commonly associated with neglect, which lie in the territory of the middle cerebral artery.^{2–5} Neglect was most often associated with larger lesions that extended beyond the occipital lobe into the medial temporal lobe, up to and including the hippocampus (fig 1A). However, smaller lesions were associated with neglect in two patients (N5 and N7), and two controls had lesions that extended into the temporal lobe up to and including the parahippocampal gyrus. Figure 1C shows the direct contrast of the areas damaged in the neglect group and those in the control group. The region most associated with neglect lay in the white matter of the occipital lobe, where damage cooccurred in all the patients with neglect but was spared in the controls.

Previous reports^{2–7} have documented neglect after isolated thalamic lesions. Thalamic damage was present in two patients with very dense neglect (N1 and N2) although, taking the series as a whole, damage to the thalamus did not appear to be necessary to cause neglect. Recently, Park *et al.*¹⁰ suggested that PCA stroke may cause neglect through combined damage to the occipital lobe and to the splenium

of the corpus callosum, as this would result in deafferentation and disconnection of one hemisphere from visual information about the contralateral side of space. A rather similar argument was also proposed by Gaffan and Hornak,¹⁹ and equivalent proposals have been used to explain pure alexia after left-sided PCA infarction.²⁰ Four patients in our study had lesions to these areas and all four had rather dense neglect. Nevertheless, there were four patients with neglect in whom there was no involvement of the splenium, and neglect without splenial damage was also reported in the Park *et al.*¹⁰ study. Thus, similar to the thalamus, damage to the splenium does not seem to necessarily cause neglect. However, damage to both of these areas, as well as the overall volume of the lesion, may have a role in determining the severity of neglect after PCA infarction.

Our data point towards a critical role for white matter in the occipital lobe. Although the study by Mort *et al.*⁷ identified an area in the parahippocampal gyrus that was most associated with neglect, our findings suggest that more posterior lesions in the white matter may suffice to cause neglect. A recent investigation using DTI in healthy humans has shown that the parahippocampal area has strong reciprocal connections with the angular gyrus⁸—an area strongly associated with neglect.⁵ This tract resembled the inferior longitudinal fascicle, a well-categorised white matter tract connecting these areas in the macaque.⁹ Critically, the fibres seem to course through the white matter of the posterior occipital lobe, including the region identified to be associated with neglect in our study (fig 2A). Importantly, the areas most commonly damaged in the controls do not lie within this tract (fig 2B). The parahippocampal region and the posterior parietal cortex play a critical role in the representation of large scale space.²¹ Thus, a unilateral disconnection of these brain areas may cause neglect, at least in the acute stage. Disconnection has also been considered to underlie neglect following damage to parieto-frontal connections.^{22–23}

Six of the patients were assessed on additional tests of visual perception. There was no evidence of impairment in figure-ground segregation, which is considered to be an early (precategorical) visual process.²⁴ However, there was evidence for impairment of varying severity at the level of perceptual identification (table 2). Impairment on these tests is usually associated with damage to the lateral aspect of the right parietal lobe—not the medial occipitotemporal regions damaged in these patients.^{25–26} Complex visual perception has been proposed to be dependent on the interaction between information carried in the ventral visual stream and the inferior parietal lobe in the right hemisphere.²⁷ Our data are consistent with this, although further research is necessary to characterise the neural underpinnings of object perception more precisely.

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