Visual neglect after right posterior cerebral artery infarction

C M Bird, P Malhotra, A Parton, E Coulthard, M F S Rushworth and M Husain

J. Neurol. Neurosurg. Psychiatry 2006;77;1008-1012; originally published online 13 Jun 2006; doi:10.1136/jnnp.2006.094417

Updated information and services can be found at:
http://jnnp.bmjjournals.com/cgi/content/full/77/9/1008

These include:

References
This article cites 23 articles, 12 of which can be accessed free at:
http://jnnp.bmjjournals.com/cgi/content/full/77/9/1008#BIBL

Rapid responses
You can respond to this article at:
http://jnnp.bmjjournals.com/cgi/eletter-submit/77/9/1008

Email alerting service
Receive free email alerts when new articles cite this article - sign up in the box at the top right corner of the article

Notes

To order reprints of this article go to:
http://www.bmjjournals.com/cgi/reprintform

To subscribe to Journal of Neurology, Neurosurgery, and Psychiatry go to:
http://www.bmjjournals.com/subscriptions/
Visual neglect after right posterior cerebral artery infarction

C M Bird, P Malhotra, A Parton, E Coulthard, M F S Rushworth, M Husain

J Neurol Neurosurg Psychiatry 2006;77:1008–1012. doi: 10.1136/jnnp.2006.094417

Visual neglect is a frequently observed syndrome after unilateral brain damage, characterised by a failure to respond to contralesional stimuli. 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. Neglect has also been reported after lesions of the thalamus, but it is 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 addressed only recently by Mort et al. 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 parietotemporal white matter tract that connects the same regions in non-human primates. A second study by Park et al. 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. 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). 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
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). 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 Corporal 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 test, 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.14 Personal neglect was rare, with only two patients failing the razor test (N1 and N2) and only one of these also failing the...
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. Both of these areas have been associated with visual neglect. Although we found no area of overlap close to the parahippocampal gyrus, it is

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Performance on the tests of visual perception</th>
</tr>
</thead>
<tbody>
<tr>
<td>ID</td>
<td>N2</td>
</tr>
<tr>
<td>Interval (days)*</td>
<td>44.00</td>
</tr>
<tr>
<td>Shape detection</td>
<td>19/20 (pass)</td>
</tr>
<tr>
<td>Fragmented letters</td>
<td>7/20 (&lt;5 centile)</td>
</tr>
<tr>
<td>Silhouettes</td>
<td>4/30 (&lt;5 centile)</td>
</tr>
</tbody>
</table>

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

*Interval between stroke and assessment.

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).
possible that lesions within the white matter of the occipital lobe disrupt the tract identified by Rushworth et al. 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 gyrus. 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. 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 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. suggested that PCA stroke may cause neglect through combined damage to the occipital lobe and to the thalamus of the corpus callosum, as this would result in deafferentation and disconnection of one hemisphere from visual information about the contralesional side of space. A rather similar argument was also proposed by Gaffan and Hornak, and equivalent proposals have been used to explain pure alexia after left-sided PCA infarction. 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. 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. 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 gyrus—an area strongly associated with neglect. This tract resembled the inferior longitudinal fascicle, a well-categorised white matter tract connecting these areas in the macaque. 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. 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.

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. 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. 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. Our data are consistent with this, although further research is necessary to characterise the neural underpinnings of object perception more precisely.

ACKNOWLEDGEMENTS

We thank the patients who participated and the Wellcome Trust for funding this research. CMB is funded by a Medical Research Council co-operative grant to the Institute of Cognitive Neuroscience, University College London.

Authors’ affiliations

C M Bird, P Malhotra, E Coulthard, M Husain, Institute of Cognitive Neuroscience, University College London, London, UK
A Parton, Centre for Cognition & Neuroimaging, Brunel University, Middlesex, UK
E Coulthard, M Husain, Institute of Neurology, University College London
M F S Rushworth, Department of Experimental Psychology, University of Oxford, Oxford, UK

Competing interests: None declared.
REFERENCES