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SHORT REPORT

# Neuropsychological consequences of two patterns of brain damage shown by MRI in survivors of severe head injury

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**Abstract**

**Two subgroups of patients were identified from 48 patients with traumatic head injury who had MRI during the acute stage: (*a*) those with severe diffuse injury—six patients with lesions in both the corpus callosum and the brain stem; (*b*) those with severe focal injury—16 patients with extensive frontotemporal lesions. Most patients with diffuse injury were in a coma on admission to hospital, whereas most patients with focal injury were out of coma. Duration of post-traumatic amnesia was prolonged in both groups. Patients were followed up at six months after injury, when a battery of neuropsychological tests was given. Patients with both diffuse and focal patterns of injury were impaired by comparison with controls on a range of measures, including tests of memory and attention. The findings contrast with the view that diffuse injury is of much greater importance than focal injury in determining outcome after head injury.**

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In recent years evidence has accumulated from neuropathological work on head trauma that patients with focal and diffuse injury should be distinguished.[1–3] Focal injuries include haematomas and contusions, whereas diffuse axonal injury is characterised by three features: lesions in the corpus callosum, lesions in the brain stem and, at a microscopic level, diffuse axonal damage. Vascular and hypoxic or ischaemic damage can also cause focal and diffuse patterns of lesions. The distinction between focal and diffuse injury has important implications for acute management and is also often used to characterise survivors. Unfortunately, the criteria used to distinguish diffuse from focal injury in survivors have shortcomings; in particular, diffuse injury is often defined negatively by the presence of coma without mass lesions on CT.[4 5]

Magnetic resonance imaging is more able than CT to disclose traumatic brain damage and displays characteristic patterns of lesions. Many survivors of head injury have multiple hemispheric lesions, particularly affecting orbitofrontal regions, frontal regions, and the temporal poles,[6–8] reminiscent of severe contusions often found by neuropathology. Magnetic resonance imaging also detects lesions in the brain stem and corpus callosum[6 9] in a distribution that suggests the macroscopic signs of severe diffuse axonal injury as defined by neuropathology.[1]

The neuropsychological consequences of diffuse and focal injuries are not well understood, and a matter of controversy. Adams and colleagues have stressed the importance of diffuse axonal injury rather than focal injury in determining disability after head injury.[10] Diffuse injury is associated with prolonged coma, and Adams and colleagues argue that severe diffuse injury is incompatible with survival in anything better than a vegetative state.[10] In particular, any survivors with lesions in both the brain stem and corpus callosum would be expected to be profoundly impaired on neuropsychological testing. By contrast, focal contusional injuries are often thought to produce relatively little permanent disability even if the initial lesions are extensive.[11]

The present report concerns a comparison between patients with severe focal or diffuse lesions identified on MRI. We were specifically interested in the possibility that the neuropsychological effects of these two patterns of injury were different, either in the aspects of mental function affected or in the severity of the consequences. Neuropsychological assessment included a set of computerised tests designed to assess various aspects of information processing speed,[12] as well as conventional measures covering a range of psychological abilities commonly impaired in head injury.

## Patients and methods

### PATIENTS

Patients, aged between 16 and 73 (mean 35 years), were drawn from a group of 48 with closed head injuries and previously described.[13] All patients had been transferred to the regional neurosurgical unit after admission to a primary surgical unit. The level of consciousness on admission to the specialist

*Table 1 Clinical and MR findings in three groups of patients*

| | Brain stem and callosum lesions (n = 6) | Frontotemporal lesions (n = 16) | Other lesions (n = 16) |
|---|---|---|---|
| Acute stage: | | | |
| Coma duration (median hours) | 39 | 0·5 | 0·5 |
| PTA duration (median days) | 31·5 | 20·5 | 5·5 |
| Skull fracture | 3 (50) | 14 (88) | 8 (50) |
| Acute subdural haematoma | 1 (16) | 8 (50) | 2 (13) |
| Areas with MR lesions (max = 21) | 7·5 | 7·3 | 3·4 |
| Hemispheric areas with lesions (max = 12) | 3·7 | 6·4 | 2·6 |
| Follow up: | | | |
| At work | 1 (16) | 5 (31) | 9 (56) |
| Ventricular enlargement | 5 (83) | 12 (75) | 6 (38) |
| Cortical atrophy | 3 (50) | 8 (50) | 3 (18) |

Values in parentheses are %. PTA = post-traumatic amnesia.

neurosurgical unit was assessed using the Glasgow coma scale.[14] Tables 1 and 2 give the demographic details of the patients.

CONTROLS

Controls were 16 orthopaedic outpatients with no history of head injury, alcohol misuse, or major psychiatric illness.

NEUROIMAGING

Magnetic resonance imaging was carried out with a Picker Vista 1100, 0·15 Tesla resistive system operating at 6·38 MHz. An initial 2 cm thick spin echo (SE200/40) pilot image in the sagittal or coronal plane was used to determine the positions of 16 slices, each 8 mm thick, for a T2 weighted spin echo sequence (SE2000/80), and an eight slice T1 weighted inversion recovery sequence (IR1660/400/40) in the axial plane. The use of a low field system allowed patients to be imaged soon after injury: in all patients acute imaging was carried out within seven days of injury, and in most (76%) within 48 hours.

The images were reviewed by an experienced neuroradiologist who had no access to the neuropsychological test information on the patients. The brain was divided into 21 mutually exclusive regions: left and right orbitofrontal regions; left and right frontal regions; left and right temporal poles; left and right posterior temporal regions; left and right parietal lobes; left and right occipital lobes; left and right basal ganglia; genu, trunk, and splenium of the corpus callosum; left and right brain stem; and left and right cerebellum. The presence or absence of lesions in each region was noted. The follow up images were examined for evidence of ventricular enlargement and cortical atrophy. Ventricular enlargement was judged by visual inspection and by comparison with the expected size for a person of that age.

On the basis of the information from imaging in the acute phase two patterns of injury were identified: (*a*) brain stem and callosum injury: lesions present in both the brain stem (left or right) and the corpus callosum (genu, trunk, or splenium); (*b*) frontotemporal injury: lesions present in four or more of the following eight areas—left and right orbitofrontal regions, left and right frontal regions, left and right temporal poles, left and right posterior temporal regions.

*Table 2 Age adjusted means (SD) of neuropsychological measures for two groups of patients and a group of controls*

| | Brain stem and callosum lesions (n = 6) | Frontotemporal lesions (n = 16) | Controls (n = 16) | F value |
|---|---|---|---|---|
| Age | 22·7 (7·9) | 42·6 (18·4) | 34·4 (16·4) | 3·5* |
| NART | 31·7 (7·7) | 27·3 (9·2) | 21·7 (8·9) | 3·1 |
| Similarities | 14·6 (2·4) | 12·8 (5·6)† | 17·2 (3·9) | 3·3* |
| Digit span | 11·8 (2·3)† | 11·8 (1·9)† | 14·2 (1·4) | 7·0** |
| Vocabulary | 38·3 (11·8) | 38·5 (14·5) | 49·7 (15·6) | 2·5 |
| Digit symbol | 27·5 (7·2) | 44·2 (19·9)† | 61·1 (8·6) | 14·5*** |
| Block design | 30·9 (9·2) | 29·2 (12·3) | 36·0 (6·8) | 1·9 |
| Object assembly | 22·5 (8·4) | 24·4 (9·7) | 29·0 (6·8) | 2·3 |
| Word fluency | 28·3 (6·9)† | 34·9 (11·9)† | 49·3 (9·5) | 11·1*** |
| Logical memory | 10·8 (3·3) | 10·5 (3·7) | 13·1 (3·5) | 2·4 |
| Associate learning | 14·1 (2·0) | 13·8 (4·0) | 16·2 (3·3) | 1·9 |
| Rey copy | 31·3 (3·1) | 32·3 (9·1) | 35·5 (1·6) | 2·1 |
| Rey recall | 14·1 (5·9)† | 20·4 (8·7) | 23·5 (5·2) | 5·3** |
| Change detection threshold (ms) | 114 (140) | 64 (82) | 38 (10) | 1·6 |
| Movement detection (correct out of 30) | 24·0 (5·4) | 24·2 (8·1) | 28·0 (5·4) | 1·4 |
| Word recognition threshold (ms) | 117 (72)† | 70 (29) | 42 (7) | 7·5** |
| Simple RT (ms): | | | | |
| Decision time | 318 (73) | 326 (59)† | 273 (38) | 4·3* |
| Movement time | 247 (82) | 315 (128)† | 220 (44) | 3·9* |
| Choice RT (ms): | | | | |
| Decision time | 371 (105)† | 369 (68) | 306 (40) | 4·2* |
| Movement time | 264 (90) | 306 (126)† | 215 (48) | 3·5* |
| Visual search (ms) | 5904 (1327)† | 4241 (1942)† | 3145 (511) | 8·8*** |
| Pattern span (blocks) | 7·9 (1·2)† | 8·1 (1·6) | 9·6 (1·5) | 6·1** |
| Path span (blocks) | 5·0 (0·5) | 5·2 (0·8) | 5·5 (0·6) | 1·5 |
| Pattern learning (total items) | 147 (26) | 159 (37) | 168 (25) | 2·1 |
| Path learning (total items) | 78 (20) | 79 (37) | 98 (12) | 2·9 |

*P < 0·05; **P < 0·01; ***P < 0·001 (ANCOVA controlling for the effects of age).
†P < 0·05 (patients *v* controls, Scheffé test).

NEUROPSYCHOLOGICAL ASSESSMENT

Patients were followed up five to 12 months after injury (median six months). Neuropsychological assessment was carried out on the same occasion as follow up MRI. Patients were given a structured interview to elicit background information and determine the duration of post-traumatic amnesia. The neuropsychological test battery consisted of the following procedures. The national adult reading test (NART) was used to estimate premorbid IQ.[15] General intellectual abilities were measured using six subtests of the Wechsler adult intelligence scale (WAIS),[16] three from the verbal scale: similarities, digit span, and vocabulary; and three from the performance scale: block design, digit symbol, and object assembly. Verbal memory and learning were assessed from two subtests of the Wechsler memory scale[17]: logical memory, and associate learning. Visuoperceptual ability and visual memory were assessed by the Rey figure copy and immediate recall.[18] A word fluency test[19] was used to assess expressive aspects of language. The following computerised measures were used: change detection threshold, movement detection, word recognition threshold, simple and choice RT, visual search[12]; pattern span, path span, pattern learning, path learning.[20]

## Results

Three patients had normal images on acute MRI, and four had images which were not of diagnostic quality; these patients are not included in the analysis. The following patterns of injury were present in the 41 remaining patients: brain stem and callosum lesions (six patients); frontotemporal lesions (16 patients); brain stem and callosum lesions and frontotemporal lesions (three patients); other patterns (16 patients). The last group comprised patients who did not fall into either of the first two categories, and included those with lesions in fewer than four frontotemporal areas, and patients with lesions in either the brain stem or callosum but not both. Only three patients had both brain stem and callosum and frontotemporal injuries. Further analysis concentrated on the following groups: (*a*) six patients with brain stem and callosum lesions and without extensive frontotemporal lesions; (*b*) 16 patients with extensive frontotemporal lesions; and (*c*) 16 patients with neither of the above patterns.

### ACUTE STAGE

Table 1 gives the duration of coma and other findings in the acute stage. Coma is defined here as a Glasgow coma scale score less than or equal to 8. Most (four of six) patients with brain stem and callosum injury were in a coma on arrival at the neurosurgical unit, whereas most (12 of 16) with frontotemporal injuries were out of coma. The median duration of coma was 39 hours for patients with brain stem and callosum lesions, and less than one hour for both of the other groups (Kruskal-Wallis one way analysis of variance (ANOVA) $H = 6{\cdot}4$, $P < 0{\cdot}05$). The brain stem and callosum injury and frontotemporal injury groups had many more areas with lesions present than patients with other lesion patterns (Kruskal-Wallis ANOVA, $H = 19{\cdot}2$, $P < 0{\cdot}001$). There was also a significant difference in the number of hemispheric lesions in the groups (Kruskal-Wallis ANOVA, $H = 23{\cdot}4$, $P < 0{\cdot}001$), the frontotemporal injury group having more hemispheric lesions than either of the other two groups.

### FOLLOW UP

There was a significant difference between the groups in the duration of post-traumatic amnesia (Kruskal-Wallis one way ANOVA, $H = 12{\cdot}1$, $P < 0{\cdot}005$). Patients in both the brain stem and callosum injury and frontotemporal injury groups had longer median post-traumatic amnesias than patients with other lesions (table 1).

Table 2 shows the mean ages and NART error scores of the two groups of patients and the controls. Analysis of variance disclosed significant differences in the ages of the three groups; however, there were no differences between the groups in premorbid ability as estimated by the NART. The data were, therefore, analysed by analysis of covariance (ANCOVA), controlling for the effects of age. Post hoc testing for significant differences between groups was carried out with the Scheffé test when the omnibus F was significant. Both groups of patients were impaired on digit span, digit symbol, and word fluency. Patients with frontotemporal lesions were significantly impaired on similarities, and patients with brain stem and callosum lesions were significantly impaired on recall of the Rey figure. On the computerised tests both groups of patients were significantly impaired on visual search. Patients with brain stem and callosum lesions were impaired on word recognition threshold. Patients with frontotemporal lesions had slow decision and movement times on simple reaction time, and slow movement times on choice reaction time. Patients with brain stem and callosum lesions had slow decision times on the choice reaction time task, and were impaired on pattern span. Comparison of the two groups of patients by the Scheffé test yielded significant differences on only two tests. Patients with brain stem and callosum lesions performed less well than the frontotemporal group on digit symbol and word recognition threshold.

## Discussion

Features distinguishing patients with focal and diffuse injuries in fatal cases were described by Adams *et al.*[3] In patients with focal injuries there is a high incidence of skull fracture, intracranial haematoma, and a lucid interval before death. Patients with diffuse axonal injury have a lower incidence of fracture of the skull and intracranial haematoma. Furthermore, patients with severe diffuse head injury have less severe contusions, and rarely have a lucid interval. It is reasonable to equate the absence of a lucid interval in fatal cases with prolonged disturbances of consciousness in survivors. Table 1 suggests that the features of the two groups identified in the present study conform to the focal and diffuse groups described by Adams *et al.*[3] It should also be noted, however, that, unlike the groups described by Adams *et al*,[3] there was a significant difference in the ages of the groups with brain stem and callosum lesions and frontotemporal injury. Our findings do not assume an exact correspondence between the injuries defined by MRI and patterns of damage identified by neuropathology, but do suggest that a distinction analogous to that used in neuropathology can be applied to survivors.

The findings of the present study question the view advanced by Adams and colleagues concerning the significance of brainstem and callosum lesions, and the general importance of diffuse injury, rather than focal injury, in determining outcome.[10] Neuropathological work led to the expectation that combined brain stem and callosum lesions would be seen rarely if at all in non-vegetative survivors.[1 10] Follow up neuropsychological testing of survivors with these lesions, however, did not confirm this expectation. All patients with these lesions were testable, and overall impairment was similar to that found in patients with focal lesions.

The present study is consistent with the idea that both focal and diffuse injuries contribute to outcome,[21 22] and that these injuries may occur in different subgroups of patients with head injuries. Diffuse injury was associated with prolonged coma, whereas post-traumatic amnesia was prolonged for both types of injury. At follow up, there were both similarities and differences in the groups on neuropsychological testing. The results suggest that patients with diffuse injuries show slowing of information processing which is central in origin. It is premature, however, to comment in detail on neuropsychological differences between the groups.

Interpretation is complicated by the small number of patients in the diffuse group and the age differences between the subgroups. A further problem is the need to match severity of focal and diffuse injuries. A measure such as the Glasgow coma scale is appropriate for measuring severity of diffuse damage; however, it does not, and was never intended to, index the severity of focal injury. It is not clear how the severity of focal injuries should be assessed, and how such a measure should be related to the severity of diffuse damage. The present report points to the need for further work to investigate these issues.


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