

CASE STUDY

Injury and recovery: Severe amnestic syndrome following traumatic brain injury

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Abstract

Primary objective: To illustrate the clinical course of a patient with a marked amnestic syndrome resulting from a closed head injury that had significant effects on frontal and thalamic memory structures.

Methods and procedures: The patient underwent a series of brain imaging investigations (CT and MRI) and neuropsychological investigations to determine the severity and course of behavioural and cognitive impairments.

Results: Three months post-injury, the patient demonstrated dense retrograde and anterograde amnesia for auditory-verbal and visuo-spatial information, disorientation and confabulation. In contrast, memory for faces appeared unimpaired. One month later the patient's behaviour, orientation and spatial memory had improved with no concomitant improvement in auditory-verbal memory.

Conclusions: The findings indicate that injury to the diencephalon manifests in a verbal amnesic syndrome that is anterograde in nature if localized in the region of the anterior left thalamus, but leaves a relatively intact visual memory. Furthermore, injuries to the frontal and temporal lobes and their projections to the diencephalon may be more important in the emergence and resolution of retrograde amnesia and disturbances in autobiographical recall than previously appreciated.

Keywords: Amnesia, traumatic injury, diffuse axonal injury

Introduction

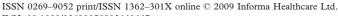
Amnesia is a recognized consequence of injury to the major structures of the diencephalon. Squire and Moore [1] vividly described N.A., a patient with a marked amnesia resulting from a fencing foil that entered the right nostril and went across the mid-line towards the left thalamus. Several other cases of penetrating thalamic injuries have since followed [2]. These and other cases have shown that thalamic injuries can result in a clinical syndrome comprising dense retrograde and anterograde amnesia, confabulation and severe personality changes. However, amnesia is also a recognized consequence of frontal and temporal lobe injury [3-5] to which the thalamus is intimately connected via reciprocal

cortico-subcortical connections. The rarity of discrete injuries to the thalamus has prevented a comprehensive and complete clinical profile of the thalamus and its cortical connection in the emergence and resolution of amnesia [6, 7]. This study reports the course and outcome of an unusual case of closed head injury that resulted in a deep thalamic haemorrhage and marked amnestic syndrome.

Case report

DD is a 26 year old university graduate in medical instrumentation who had worked in the human resources department in a large rehabilitation hospital. He was found unconscious on the

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road by a passer-by. As he was found near his cycle with a protective helmet on, it was presumed that he was a victim of a hit-and-run collision. Glasgow Coma Scale (GCS) at the scene of the accident was 3, rising to 7 on admission. Upon arrival at the hospital preliminary investigations showed lacerations and bruises to the right shoulder and face with blood in the right ear. A Computer Tomography (CT) brain scan showed multiple petechial haemorrhages, haemorrhage in the corpus callosum and bifrontal heamorrhages. Figures 1 and 2 show CT images taken 24 hours after the accident and show evidence of a deep heamorrhage of the right frontal lobe and a small haemorrhage in the postero-lateral left thalamus, respectively. He was sedated, intubated and an external ventricular drain (EVD) was inserted. The EVD was removed 6 days later and he was reported to be responding well and obeying commands, but with some left-sided weakness.

The patient was transferred to a rehabilitation hospital 2 weeks following injury and underwent a Magnetic Resonance Imaging (MRI) scan. A 1 cm haematoma was found adjacent to the corpus callosum in the region of the velum interpositum. A series of small 5 mm haemorrhages were seen in the right frontal white matter and a small haemorrhage in the postero-lateral left thalamus. Cortical contusion of the left temporal pole was also reported. No mass effect was seen. Multiple foci of blooming were seen on gradient echo images at grey/ white matter interfaces in keeping with diffuse axonal injury. Bilateral subdural collections were seen to overlie the frontal and temporal convexities, measuring 8 mm on the right and 7 mm on the left. There was no evidence of blooming on the gradient echo, suggesting traumatic subdural hygromas rather than subdural haematoma.

On admission to rehabilitation he was disoriented to person, place and time. His information processing was slow and he was repetitive in conversation. Formal assessment of post-traumatic amnesia (PTA) commenced 5 days after admission. In the following 30 days, DD maintained fluctuating scores of 6-7 out of 12 on the Westmead PTA Scale and remained at 7/12 on discontinuation. Subsequently, his sleep wake cycle settled and his attention was more stable. Based on this, his estimated length of PTA was 49 days, although it is noted that this figure was somewhat arbitrary in the presence of ongoing memory disturbance.

A follow-up CT scan 2 months after injury showed significant decrease in the size of subdural collections measuring \sim 3 mm in depth on the right side and almost complete resolution on the left side. Intraparenchymal abnormalities shown on MRI could not be visualized on the CT. He was seen for neuropsychological assessment ~3 months following the initial injury.



Figure 1. Computed Tomography (CT) axial scan without contrast performed on the 24 hours following injury showing a small haemorrhage in the right basal ganglia.



Figure 2. Computed Tomography (CT) axial scan without contrast performed on the 24 hours following injury showing a small haemorrhage in the left postero-lateral left thalamus.



Neuropsychological assessment

During the neuropsychological assessment DD's speech was highly repetitive and grossly confabulatory. In one 2-hour session, he repeated the same joke more than 10 times, identically and with variations. DD showed no real orientation to time and exhibited a marked retrograde amnesia. His orientation to place was similarly impaired and fluctuated between the belief that he was on a school camp (although he was 26 years of age at the time) or being at University. He had no recollection of being in hospital or having been told he had been in an accident. He was unaware of any problems with his cognition or memory.

On formal review, DD demonstrated evidence of at least average range pre-morbid IQ (Table 1). More routine information processing and routine mental operations, such as counting upwards, remembering the days of the week or months of the year was intact. Speed of information processing was relatively slow, but not abnormal.

There was no indication of visual agnosia, visuoperceptual or visuo-constructional impairments. His auditory working and spatial memory was within normal limits.

Table I. Neuropsychological test scores expressed as raw, z-scores and estimated percentiles.

Cognitive domain/test	March				April			
	Raw score	Scaled	z-score	%	Raw	Scaled	z-score	%
Pre-morbid IQ								
WTAR	36	105	+0.15	55	_	_	_	_
Matrix reasoning	18	11	+0.15	55	_	_	_	_
Visuo-perception								
Block design	49/68	12	+0.5	69	_	_	_	_
Rey complex figure test	4		< 3.0	<1	12.5	_	+1.41	92
Attention/speed								
Mental control	20	7	-1.0	15	_	_	_	_
Trails A	29	_	-0.16	44	_	_	_	_
Trails B	96	_	-2.38	<1	_	_	_	_
Symbol search	25	7	-1.0	16	_	_	_	_
Digit symbol—coding	56	6	-1.6	5	_	_	_	_
Memory								
Digit span-forward	10	10	0.0	50	10	10	0.0	50
Digit span-backward	8				7			
Word list memory								
Total	22	4	-2.0	2	21	4	-2.0	2
Delayed recall	0	4	-2.0	2	9	1	-3.0	<1
Delayed recognition	0	1	-3.0	<1	_	_	_	_
Logical memory I	20	4	-2.0	2	29	7	-1.0	15
Logical memory II	2	1	-3.0	<1	0	1	-3.0	<1
Spatial span-forward	6	6	-1.6	5	8	8	-0.7	25
Spatial span-backward	6				7			
Face memory I	34	8	-0.4	35	_			_
Face memory II	30	6	-1.6	5	_	_	_	_
CVMT								
Total score	55	_	-3.0	<1	78	_	-1.0	15
Delayed recognition	3	_	-2.13	2	4	_	-1.2	12
Conceptual/abstract reasoning	•							
Similarities	24	11	+0.3	60	_	_	_	_
Picture completion	20	9	-0.2	40	_	_	_	_
Wisconsin card sorting test	(WSCT-64)							
Categories completed	1	_	_	2-5	_	_		_
Trials to 1st category	25	_	_	6-10	_	_	_	_
Total errors	34	_	_	2	_	_	_	_
Perseverative errors	18	_	_	1	_	_	_	_
Executive								
Stroop-W	89	_	0.6	73	_	_	_	_
Stroop-CN	73	_	-0.4	34	_	_	_	_
Stroop-CW	32	_	-1.3	10	_	_	_	_
Verbal fluency								
F,A,S	8/10/2	_	-2.29	<1	14/10/11	_	-0.8	20

Neuropsychological test scores presented in relation to major functional domains.



DD demonstrated a gross amnesia for auditory information. Gross impairments observed in learning the items of a 12-item word list (<10%). After a short delay he was unable to recall or recognize any of the words from the list. Similarly, he was unable to recall any items of two prose passages after a 30-minute delay. Visuo-spatial recall was also impaired, although he was able to remember elements of a complex figure after a delay.

Higher order functions showed no abnormality in visual or verbal abstract reasoning. His ability to inhibit over-learned responses was significantly impaired and he had difficulty initiating new response sets on a verbal fluency task, which was also hampered by marked perseveration. Similarly, he was inflexible in shifting between competing response sets in the Wisconsin Card Sorting Task (WCST).

Follow-up

Immediately following the preliminary neuropsychological assessment a rehabilitation strategy was started that attempted to capitalize on DD's better visuo-spatial memory in order to aid his orientation. He was required to choose a photograph from the newspaper each day and attempt to recall three facts associated with the picture. Other visual strategies were employed such as the use of visual associates to aid his recall of various therapists' names. After ~ 1 week, therapists noted improvements in orientation and understanding of environment. The severity of his retrograde amnesia was quantified by the disparity in his view of his current situation (back at a school camp or university) and the actual date. He was highly repetitive and from close monitoring it was possible to discern the approximate time at which his retrograde amnesia resolved. He was able to recall that he was in hospital and the reasons for his admission. Correspondingly there was an increase in insight, which was accompanied by a marked reduction in mood.

At 4 months post-injury a further assessment was conducted to determine his insight and orientation. He was able to correctly recall the year and was close to recalling the day and date correctly. He was able to recall the names of recent political figures and an account of the previous 4 years of employment since leaving university. He was no longer confabulating, less preservative and less prone to tangents in conversation. He could recall details he had been told about the accident, including the date. Despite these improvements, he remained highly repetitive in conversation. On testing of visuo-spatial memory, he showed marked improvements in both new learning and recognition memory, but there was no comparable change in auditory verbal learning or memory and he was unable to recall or recognize any previously presented auditory verbal material.

Discussion

Traumatic injury to the thalamus is known to result in marked neurocognitive, behaviour and personality change. In particular, memory disorders including retrograde and anterograde amnesia are commonly reported [6, 8–11], as well as aphasia [12, 13], frontal disinhibition [14], motor problems [15], severe personality changes [16, 17] and hypersexuality [18].

In the present case, there was extensive injury to the left thalamus but no corresponding disturbance or injury to the right thalamus in the context of bifrontal haemorrhage and temporal contusion. Despite the apparent lifting of post-traumatic amnesia at 2 months post-injury, as evidenced by a return to normal sleep-wake cycle and intact attention, the patient remained disoriented and grossly confabulatory at 3 months post-injury with a pervasive retrograde amnesia and dense anterograde amnesia for both auditory-verbal and visualspatial information. By 4 months, the rehabilitation team recorded significant improvements in DD's mental state—although not formally measured, his retrograde amnesia clearly subsided and he was oriented. With this improvement there was an accompanying resolution of the amnesia for visuospatial material but DD remained densely amnesic for auditory-verbal material.

DD demonstrates the unpredictable nature and time course of recovery following thalamic injury. Despite the resolution of disorientation, confabulation and retrograde amnesia, the injury to the left thalamus left a pervasive and persistent episodic impairment that did not resolve by the time of follow-up or, anecdotally, in the 3 years since his injury. In a previous case study, Parkin et al. [8] described a similar patient following a left thalamic infarction who developed a severe episodic amnesia with a profound deficit in verbal memory in the context of normal intelligence. Such severe impairment was considered possible only if the lesion, localized to the anterior thalamus, interfered with the hippocampal pathway and either the amygdala pathway or the pathway starting from the perirhinal cortex and ending at the dorso-medial nucleus. Other studies have implicated only the left mammillothalamic tract and left mediodorsal nucleus in verbal episodic amnesias [9, 10, 14]. It is therefore apparent that in DD's case the large haemorrhage of the left thalamus resulted in the dense auditory verbal amnesia, yet left visuo-spatial memory



unaffected. In a similar case, Schott et al. [19] described a man who was recruited as a control subject for a longitudinal MRI study and later sustained a left thalamic infarct during the course of the study. Information was available on his premorbid cognitive status and a brain scan had been conducted which was normal at the point of recruitment. Like DD, this patient experienced selective episodic memory impairment for verbal material and poor recall of names of famous faces, despite good recognition and preserved visual memory. Both cases provide clear evidence of lateralization of memory processing at the subcortical level of the thalamus.

This case highlights the potential role of corticothalamic structures in the emergence and resolution of some of the key symptoms that follow severe head injury including disorientation, autobiographical memory loss, confabulation and retrograde amnesia. Although these features are sometimes also found in delirium states with or without concomitant brain injury, they are also common in a range of disorders that primarily affect fronto-cortical and diencephalic atrophy. For instance, confabulation, the generation of false memories in the context of amnesia, occurs in many disorders that involve compromise of memory control functions particularly where the orbitofrontal and ventromedial cortex is damaged [20, 21], and several studies have shown the resolution of confabulation with the return of normal perfusion to the frontal cortex and improvement in frontal/executive function [22, 23]. In line with this DD's confabulation resolved with signs of improvement in frontal/executive function, including increased insight, reduced perseveration tangentiality.

The memory components of past recall also rely on the intact functioning of cortico-thalamic transmission. The anteromesial thalamus, including the mammillo-thalamic tract and dorsomedial nucleus, have rich projections to frontal and temporal regions of the brain, which play a crucial role in memory formation and retrieval of past memory [9, 14, 24, 25]. In particular, the right mediodorsal region of the thalamus is believed to play a specific role in accessing autobiographical and semantic details, autobiographical incidents and some aspects of world knowledge [9, 24]. Several recent studies have suggested that damage to lateralized diencephalic structures, particularly the right mediodorsal nucleus, right mammillothalamic tract, posteromedial region as well as left mediodorsal nucleus and bilateral internal medullary lamina are necessary to invoke retrograde memory loss [9, 10, 14, 26, 27]. In DD's case, however, there was no discernable injury to the right thalamus and correspondingly he could access considerable autobiographical detail from his life prior to the 4 years he had 'lost' to retrograde amnesia. It is interesting that this later improved as the injury to the frontal and temporal lobes resolved, which supports the view that frontotemporal cortical integrity and projections to the diencephalon are equally important as the thalamus itself in ensuring ongoing recall.

The notion that cortical insult or an interaction between cortical and diencephalic injury can cause retrograde amnesia is not unprecedented. Kopelman et al. [28] examined retrograde amnesia in patients with diencephalic, temporal lobe or frontal lesions and found that two patients with focal dicencephalic lesions and anterograde amnesia did not demonstrate problems in accessing remote memory. In contrast, patients with frontal lobe lesions were more impaired in recall of autobiographical and famous news events, whilst those with temporal lobe lesions demonstrated a similar impairment, albeit with a 'flat' temporal gradient. In DD's case, the resolution of subdural hygromas and the deep right frontal lobe heamorrhage appears to correspond to the lifting of retrograde amnesia and, given that his right thalamus was intact, suggests that cortical insult plays a greater role in the emergence and also the resolution of retrograde amnesia than may have been previously appreciated.

In conclusion, while the present case study offers further evidence of the specific anatomical correlates of functional pathologies in memory, it also highlights the fact that memory relies upon a complex network of cortical and subcortical structures. While irreversible damage to these structures may lead to debilitating memory deficits, the distributed nature of the network may also permit intact structures to be tapped in order to help patients cope with their disabilities. In DD's case, his intact visual memory served as an anchor point for a rehabilitation programme that has been used to assist his reintegration. Although he still faces intractable problems with auditory verbal learning and recognition, his day-to-day functioning has improved through the use of external visual aids in the form of a Personal Digital Assistant (PDA), notes and alarms. He has now resumed employment on a parttime basis in a hospital department of records.

Declaration of interest: The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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