SHORT REPORT

Retrograde temporal order amnesia resulting from damage to the fornix

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Abstract

Some amnesic patients show an impairment of temporal order memory that cannot be accounted for by content memory deficits. The performance of an amnesic patient on memory tasks assessing the patient's content and temporal memories for remotely acquired material is described, after a lesion including the bilateral anterior fornix and adjacent anterior thalamus. The patient displayed a deficit in the temporal order tasks for remotely acquired information. Neither frontal cognitive deficits nor recognition deficits can account for this patient's poor temporal memory. This retrograde temporal order memory impairment without content memory deficits were not seen in previously reported thalamic amnesic patients. Accordingly, the present patient's poor retrograde temporal memory could hardly be explained by only a thalamic lesion. It is concluded that the patient's impairment of temporal order memory for the retrograde material is probably due to the direct disconnection between the frontal lobe and the hippocampus by disruption of the fornix.

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Keywords: fornix; thalamus; amnesia; temporal order

Previous studies have indicated that some amnesic patients have an impairment of temporal order memory, and it was suggested that different brain structures such as the limbic-diencephalic and frontal regions may contribute to the process that underlies temporal memory, but each may do so in different ways.¹ The fornix is known to connect these temporal memory related regions,²⁻⁴ and there are several reports in the literature on memory disorders after fornix lesions in humans.⁵⁻⁷ However, the effect of a fornix lesion on temporal order memory has not yet been elucidated. Here we report on a patient who developed retrograde temporal order amnesia after a lesion including the bilateral fornix.

Method

CASE REPORT

A 51 year old right handed high school educated woman was admitted to our hospital in November 1995, after an episode of disorientation, amnesia, headache, nausea, and vomiting. Brain CT and MRI disclosed a cavernous haemangioma situated in the anterior part of the third ventricle with obstructive hydrocephalus. A fenestration of transparent septum and placement of a ventriculoperitoneal shunt for the hydrocephalus were performed. The tumour was not resected, to prevent hemorrhage. There were no operative complications and the patient's recovery in the immediate postoperative period was uneventful.

Several weeks after the operation, she was unable to recall any of the events surrounding her illness, and showed difficulty in recent memory retrieval. Brain MRI performed 2 months after the surgery showed an area of cavernous haemangioma in the anterior part of the third ventricle (figure A). The lesion involved the bilateral anterior fornix and the anterior parts of medial thalamus (figure B, C). Single photon emission computed tomography (SPECT) carried out after the surgery showed an abnormal distribution of the tracer in the lesion, whereas in other areas its uptake was normal.

Neuropsychological evaluation

An extensive neuropsychological evaluation was performed between 2 and 5 months after the operation. The patient's scores are given in the table. There were no remarkable abnormalities except for anterograde memory deficits. The patient's retrograde memory was assessed by a structured interview covering past personal events. In addition, the famous faces and events test was administered, on which she was shown pictures and asked the names of the pictured subjects or events. In both of these tests, there was no evidence of significant retrograde amnesia.

Retrograde temporal order memory

When we asked the patient about the temporal order of the past events, she showed difficulties in both the autobiographical and the famous persons or events tests. For example, she could

tell us the details of travels with her family in the previous year and 5 years earlier, but when we asked her which event had occurred first or after the other, she made a mistake. She knew very well that a major earthquake had occurred in Japan in the previous year and that a major international airport was opened nearby 2 years earlier, both of which were very familiar events in her living area, but she could not decide which event had occurred first or second. In the temporal order tasks, she stated that she felt confused when remembering the order of the events, even though the events were familiar to her.

Experimental procedures for testing retrograde temporal order memory

Retrograde temporal order memory was evaluated using public events arrangement tasks from Bowers *et al.*⁸ For this task, items were taken from the pictures used in the famous faces or events test for the evaluation of the

patient's past event memory. A total of 40 items was used, consisting of 10 from each decade from the 1960s to the 1990s. Each item was presented on a card. For each trial, the subject was presented with a set of four cards, one for each decade, arranged in a random order. The subject was then asked to order the four events according to their time of occurrence, starting with the most remote event and completing the set with the most recent one. Ten trials were administered in this way. The accuracy of placement per decade and global arrangement score were calculated. The accuracy of placement per decade was based on the number of items per decade placed in the correct position within a set. The global arrangement score was a vector score based on the distance between the correct response and the subject's response. For each item within a set, the absolute difference was taken between the position given to the item by the subject and its correct items within a set. For example, a response (1960s,

(A) Axial view of the T2 weighted MR images of the patient's brain. The arrows indicate the lesion of cavernous haemangioma. (B) MRI of the diencephalic region (phase T2). Four coronal sections are shown, the most anterior level on the left top, the most posterior level on the right bottom. The hypodense area indicated by the arrows shows the patient's lesion (for exact location see (C)). (C) Lesions plotted on the corresponding sections in the coronal planes (first plane VCA=4 mm, second plane VCA=12 mm, third plane VCA=16 mm) from the atlas of Talairach and Tournoux.⁸ The circled areas represent the patient's lesion. Bo=Optic tract; Cc=corpus callosum; Cm=mamillary body; Fo=fornix; Hy=hypothalamus; Nc= caudate nucleus; Nr=red nucleus; Ns= subthalamic nucleus; Sn=substantia nigra; Th=thalamus; na= anterior nucleus; dm=dorsomedial nucleus; va=ventral anterior nucleus; vl=ventral lateral nucleus; vpl=ventral posterior lateral nucleus; VI=lateral ventricle; V3=third ventricle.

Neuropsychological test results

	Patient's scores
General intelligence	
RCPM	3 /36
WAIS-R (v-IQ/p-IQ/f-IQ)	96/87/91
Token test ⁹	99% correct
Frontal function	
WCST (category achieved)	5
Stroop test (interference) ¹⁰	42 per 45 seconds
Word fluency ¹¹	13 per minutes
Memory	
Digit span	
forward	7
backward	4
RAVLT-R	
Trials 1-5	3, 7, 7, 6, 8
Postinterference	4
30 minutes delayed recall	3
30 minutes delayed recognition	15
Benton visual reproduction (trial A) ¹²	7
WMS-R	
General memory index	79
Verbal memory index	67
Visual memory index	112
Attention/concentration index	102
Delayed index	62
Logical memory raw scores	
Immediate	10 (20 percentile)
Delayed	0 (0 percentile)
Visual reproductions raw scores	
Immediate	37 (90 percentile)
Delayed	15 (37 percentile)

RCPM=Raven's coloured progressive matrices¹³; WAIS-R=Wechsler adult intelligence scale revised¹⁴; WCST=Wisconsin card sorting test¹⁵; RAVLT-R=Rey auditory verbal learning test revised¹⁶; WMS-R=Wechsler memory scale revised.¹⁷

1980s, 1970s, 1990s) would receive a score of 0 +1 +1 0. The scores were then summed across 10 trials. These same tests were administered to nine normal controls who were matched as closely as possible for age and educational level (mean age=51.3 years). Informed consent was obtained from all subjects before they participated in these experiments.

Results

The patient's overall global arrangement score was 18, which was significantly greater than that of the control group (mean 6.0 (SD3.2)). For the percentage accuracy of placement scores across each decade, there was a significant difference in the performance of the patient and the controls for events of the 1960s and 1970s. The patient's accuracy for other decades was also below that of the control group, although not significantly so (1960s: the patient=60% *v* controls=83% (SD 5%); 1970s: 40% *v* 74% (SD 9%); 1980s: 70% *v* 86% (SD 15%); 1990s: 90% *v* 96% (SD 7%)).

Discussion

Our major finding was that she displayed a deficit in the temporal order tasks for remotely acquired information. The temporal memory deficits displayed by this amnesic patient cannot be ascribed to cognitive deficits associated with frontal lobe dysfunction. She performed normally on non-memory cognitive tasks of frontal lobe functioning, and neuro-radiographic studies showed no evidence of frontal lobe involvement. Likewise, her content memory for events about which she failed to make correct temporal judgments was good, indicating that her poor temporal memory was not the result of the impairment of content memory.

The lesion in the present patient included not only the fornix but also parts of the dorso-medial and anterior thalamic nuclei, so it is possible that the additional damage in the dorso-medial or anterior thalamic nuclei affected her temporal order memory. However, retrograde temporal order deficits without amnesia for content memories were not seen in the previous reports of thalamic amnesic patients.¹⁹⁻²¹ Accordingly, the present patient's retrograde temporal order memory impairment could hardly be explained by only the thalamic lesion. We consider that this patient's impairment of temporal order memory for the retrograde material is affected by the damage to the fornix.

The mechanism underlying temporal ordering is not known. Several suggestions have been made regarding possible mechanisms. Deutsch²² suggested two complementary mechanisms for making temporal judgments, one based on a summation of memory traces and one based on comparisons between traces. He does not propose specific anatomical sites for these systems, but Sagar *et al*¹ proposed that the comparator may be a frontally based system and involve mediation, whereas the summation may be more factually represented and may be based on the limbic-diencephalic system.

Damage to either system may impair temporal contextual memory, but content memory is also affected in many patients with damage to the limbic-diencephalic system. With damage to the frontally based system, the content memory is relatively preserved. This consideration is supported by the performance in content recognition and recency discrimination shown by amnesic patients.^{1 19 23}

Parkin and Hunkin²⁴ showed that impairments on anterograde measures of temporal context were due to midline diencephalic lesions, but temporal judgments about retrograde memories might depend on intact frontal lobe functioning. Their result also indicated the existence of two different complementary mechanisms for making temporal judgments in the limbic-diencephalic system and the frontally based system.

The present patient showed impaired temporal order judgment for the retrograde material that cannot be accounted for by impaired content memory, and this performance was the same as that of the patient who has damage to the frontally based system. Although the patient's lesion did not involve the frontal region, most fibres interconnecting the mesial frontal area (including the medial septal/diagonal band complex) with the hippocampal formation pass through the fornix-fimbria system,²⁻⁴ so that her lesion directly disconnected the frontal lobe and the hippocampus by disrupting the information conveyed in the fornix. This disruption might result in the present patient's retrograde temporal ordering deficit.

1 Sagar HJ, Gabrieli J, Sullivan E, *et al*. Recency and frequency discrimination in the amnesic patient H.M. *Brain* 1990;113:581-602.

2 von Cramon DY, Schuri U. The septo-hippocampal pathways and their relevance to human memory. A case report. *Cortex* 1992;28:411-22.

- 3 Swanson LW, Cowan WM. An autoradiographic study of the organization of the efferent connections of the hippocampal formation in the rat. *J Comp Neurol* 1979;172:49–84.
- 4 van Hoesen GW. Neural systems of the non-human primate forebrain implicated in memory. *Ann N Y Acad Sci* 1985;444:97–112.
- 5 Hodges JR, Carpenter K. Anterograde amnesia with fornix damage following removal of IIIrd ventricle colloid cyst. *J Neurol Neurosurg Psychiatry* 1991;54:633–8.
- 6 McMackin D, Cockburn J, Anslow P, et al. Correlation of fornix damage with memory impairment in six cases of colloid cyst removal. *Acta Neurochir* 1995;135:12–8.
- 7 Calabrese P, Markowitsch HJ, Hardes AG, et al. Fornix damage and memory. A case report. *Cortex* 1995;31:555–64.
- 8 Talairach J, Tournoux P. Co-planar stereotaxic atlas of the brain. New York: Thieme, 1988.
- 9 de Renzi E, Faglioni P. Normative data and screening power of a shortened version of the token test. *Cortex* 1978;14:41–9.
- 10 Stroop J. Studies of interference in serial verbal reactions. *J Exp Psychol* 1935;18:643–62.
- 11 Borkowski JG, Benton AL, Spreen O. Word fluency and brain damage. *Neuropsychologia* 1967;5:135–40.
- 12 Benton AL. *The revised visual retention test*. Iowa: The State University of Iowa Press, 1963.
- 13 Raven JC. Guide to the standard progressive matrices. London: HK Lewis, 1958.
- 14 Wechsler D. *WAIS-R manual*. New York: Psychological Corporation, 1981.
- 15 Berg EA. A simple objective test for measuring flexibility in thinking. *J Gen Psychol* 1948;39:15–22.
- 16 Spreen O, Strauss E. *A compendium of neuropsychological tests*. Oxford: Oxford University Press, 1991.
- 17 Wechsler D. *Wechsler memory scale-revised*. San Antonio: Harcourt Brace Jovanovich, 1987.
- 18 Bowers D, Verfaellie M, Valenstein E, et al. Impaired acquisition of temporal information in retrosplenial amnesia. *Brain Cogn* 1988;8:47–66.
- 19 Squire LR, Zola-Morgan L, Slater PC. Anterograde amnesia and memory for temporal order. *Neuropsychologia* 1981;19:75–81.
- 20 Shuren JE, Jacobs DH, Heilman KM. Diencephalic temporal order amnesia. *J Neurol Neurosurg Psychiatry* 1997;62:163–8.
- 21 Stephanic C, Assal G, Bogousslavsky J, et al. Pure amnesia after unilateral left polar thalamic infarct: topographic and sequential neuropsychologic and metabolic (PET) correlations. *J Neurol Neurosurg Psychiatry* 1994;57:27–34.
- 22 Deutsch JA. Chronomemories and amnesia. In: Squire LR, Butters N, eds. *Neuropsychology of memory*. New York: Guilford Press, 1984:157–64.
- 23 Schacter DL, Harbluk JL, Macthachlan DR. Retrieval without recollection: an experimental analysis of source amnesia. *J of Verbal Learning and Verbal Behaviour* 1984;23:593–611.
- 24 Parkin JA, Hunkin NM. Impaired temporal context memory on anterograde but not retrograde tests in the absence of frontal pathology. *Cortex* 1993;29:267–80.