SHORT REPORT

A case of frontal network amnesia

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J Neurol Neurosurg Psychiatry 2003;**74**:106–109

A 63 year old man developed an amnesic syndrome coupled with an array of "frontal lobe" signs after bilateral small subcortical infarcts. His amnesia was characterised by severe difficulty in voluntary recall of recently memorised verbal and non-verbal materials, while his recognition for the same materials was less affected. The symptoms remained unimproved at a follow up evaluation eight months after onset. Magnetic resonance imaging showed two small circumscribed lesions, one in the dorsomedial nucleus of the left thalamus and the other in a region of the right globus pallidus and anterior limb of the right internal capsule. The mammillothalamic tracts and anterior nuclei of the thalami were clearly spared bilaterally. The left dorsomedial nucleus lesion disrupted the thalamofrontal circuit, while the anterior limb lesion of the right internal capsule disconnected the same circuit by damaging part of the anterior thalamic radiation. Thus the amnesia in this patient may have been caused by disruption of the bilateral thalamofrontal circuits. This type of amnesic pathology should be separated from more conventional types of amnesia that are produced by disruption of the so called Papez circuit or the Delay-Brion memory system.

Circumscribed thalamic lesions involving the anterior paramedian area of the thalamus have been known to produce amnesia of varying severity. Bilateral damage produces severe amnesia,¹ a left unilateral lesion impairs memory for verbal materials,² and a right unilateral lesion impairs memory for non-verbal materials.³ It has also been reported that a unilateral lesion can result in modality-non-specific amnesia.¹ However, the identification of specific anatomical structures within the thalamus responsible for memory has been a matter of controversy. In many cases, damage to the mammillothalamic tracts or the anterior nuclei has been held responsible for memory loss.^{1–6} These structures are part of the well known memory circuit of the hippocampo-fornico-mammillo-thalamo-cingulate system, which is known as the Papez circuit.⁷ In other cases, damage to the dorsomedial nucleus has been considered critical for amnesia. This nucleus has massive reciprocal connections with the orbitofrontal cortex as well as with the dorsolateral prefrontal cortex. This close functional association with the frontal lobe is clearly reflected in reported cases with dorsomedial nucleus damage, in which "frontal lobe" signs are present along with amnesia.⁸ However, in many cases even small lesions inevitably involve multiple structures, making the identification of a lesion within a specific nucleus methodologically very difficult. For instance, although many reports of thalamic amnesia attribute the resultant amnesia to a dorsomedial nucleus lesion, the possibility of mammillothalamic tract involvement cannot be ruled out. To make things more difficult, there have been reports that lesions restricted to the bilateral dorsomedial nucleus do not cause amnesia.^{1–9}

Outside the thalamus, infarcts in the genu or the anterior limb of the internal capsule have been reported to cause amnesia.^{10–12} Such lesions are of theoretical interest, as the cause of amnesia in these cases has been attributed to damage to the anterior or inferior thalamic peduncles. Both peduncles contain fibres that connect the dorsomedial nucleus with the frontal lobe.

Here we report a case of amnesia coupled with frontal lobe signs. On the basis of a detailed analysis of the magnetic resonance imaging (MRI) data, we speculate that the amnesia in this case reflects an impairment of the bilateral thalamofrontal memory circuit, which is distinctly separate from the Papez circuit.

CASE REPORT

The patient was a 63 year old, right handed florist, with a 10 year history of hypertension and diabetes mellitus. In the summer of 1999, his family noticed that his memory had worsened and he began to lose his temper easily. His forgetfulness remained stable without any apparent worsening until 3 November 2000, when he suddenly fainted at a party. On the way to a local hospital, he regained consciousness. At the hospital, no neurological abnormalities were detected. Computed tomography of the brain revealed a low density area in the right internal capsule, which was interpreted to be an infarct. He was referred to our department in February 2001, where he was found to be fully conscious and cooperative, but disoriented. Physical and neurological examinations revealed a lack of spontaneity, amnesia, and slight sensory impairment in both legs. An EEG showed delta waves prevailing in the bilateral frontal and temporal regions, with basic waves of 9–10 Hz. Laboratory studies were normal except for raised blood glucose and haemoglobin A1c levels.

Neuroradiological assessment

T2 weighted (T2W) and short inversion time inversion recovery (STIR) images were obtained with a 1.0 Tesla MRI scanner (Signa; General Electric Medical Systems, Milwaukee, Wisconsin, USA). High intensity areas were seen in the dorsomedial nucleus of the left thalamus (fig 1, A–C) and in the right globus pallidus (fig 1, A-1/A-2), a portion of which extended superiorly into the anterior limb of the right internal capsule (fig 1, B-1). STIR images successfully identified the mammillothalamic tracts bilaterally as darker regions (arrows in fig 1D), which were clearly spared from damage. There was no cortical atrophy. Measurement of blood flow with ^{99m}Tc-ECD single photon emission computed tomography showed no areas of hypoperfusion.

Neuropsychological evaluation

Neuropsychological evaluations were performed between three and 11 months after the last stroke. A loss of spontaneity was evident, considering that the patient had been very active as a leader in the local community pre-morbidly. He was disoriented in time. His forward digit span was 5. His general intelligence was low average (WAIS-R VIQ, 94; PIQ, 80; FIQ,

Figure 1 Axial STIR magnetic resonance images obtained three months after onset. (A) axial section, (B) coronal section. Areas of hyperintensity are seen in the left dorsomedial nucleus and in the right globus pallidus, extending into the anterior limb of the internal capsule. (C) An enlarged view of A-1 with a mapping of the thalamic infarct in the axial plane (Hd + 8.0 mm) using the atlas of Schaltenbrand and Wahren.¹³ The lesion is located within the dorsomedial nucleus. (D) An enlarged view of A-2 featuring subcortical structures. The thalamic lesion does not involve the mammillothalamic tracts (low intensity spots indicated by arrows). A, anterior nucleus; MD, dorsomedial nucleus.

87). No apparent abnormalities were observed using the Japanese edition of the Western aphasia battery. He showed no hemispatial neglect, visual agnosia, apraxia, or disturbance in constructional ability.

His scores on frontal measures were poor in such tests as the Wisconsin card sorting test, the trail making tests, and verbal fluency tests (table 1). On the Tower of Hanoi test, he frequently broke the rules, which he was able to describe verbally, and failed to correct his errors after they were pointed out by the examiner.

Several standardised memory tests revealed anterograde amnesia for both verbal and visual tasks (table 1). Visual memory disturbance was more prominent than verbal memory disturbance in the Wechsler memory scale–revised (verbal memory index 69, visual memory index < 50). On the Rey auditory verbal learning test (RAVLT) and the Rey–Osterrieth complex figure test, recognition was better than recall. There was no false alarm on RAVLT. Autobiographical memory was preserved, as revealed in an autobiographical memory interview, except for events in the recent past that had occurred after the onset of his illness. However, chronological estimation of past events in his life was poor. For example, he was able to describe a large flower show he had produced in detail, but he was not sure whether it was before or after opening his own flower shop. In addition, he was unable to estimate the years of his parents' death. In general, when he made a wrong answer he usually hesitated before answering. Confabulation was not prevalent—at least, spontaneous confabulation as defined by Schnider *et al*¹⁴ was not observed. The mirror drawing task was given on three consecutive days to examine the procedural memory, four trials a day. The ratio between the time to complete the drawing for the first time on the first day and for the first time on the third day was 3.8 (normal range 3.7 to 4.6), which indicates that his procedural memory was preserved.

DISCUSSION

Our case was characterised neuropsychologically by the co-occurrence of a moderate amnesic syndrome and “frontal lobe” signs, which were caused by lesions in the bilateral “frontal network.” Anterograde amnesia was prominent, with recall more disturbed than recognition. Other amnesia related regions—such as the anterior nucleus of the thalamus, the mammillothalamic tracts, the frontal lobe, and the medial temporal lobe—were not affected. The possibility of a degenerative process as a cause of our patient's symptoms was ruled out by the sudden onset of his complaints, the lack of premorbid behavioural changes, and the lack of atrophic changes on MRI.

The frontal lobe signs in our patient, without obvious frontal lobe pathology, are attributable to bilateral disruption of the thalamofrontal network by lesions in the dorsomedial nucleus on the left, and in the anterior limb of the internal capsule on the right. In order to distinguish frontal lobe signs originating from lesions outside the frontal lobe proper, the recently proposed term “frontal network syndrome”¹⁵ would be appropriate.

More and more memory related impairments—such as confabulation, impairment of free recall, temporal order judgment, and source/context memory—are becoming topics of discussion in relation to frontal lobe lesions.¹⁶ In animal studies, extensive bilateral frontal lobe lesions produce severe memory impairments.¹⁷ Bilateral lesions in the magnocellular portion of the dorsomedial nucleus also cause broad memory disturbances, including disturbance in performing a scene memory task, which is said to be analogous to human episodic memory.¹⁸ It is now clear that direct projections from the rhinal cortex to the dorsomedial nucleus are limited, and are restricted to connections with the medial part of the magnocellular portion of the dorsomedial nucleus.¹⁹ Only minor memory impairment results when ablation is restricted to the medial part within the magnocellular portion of the dorsomedial nucleus, at least in monkeys.²⁰ These data suggest that amnesia caused by a lesion in the dorsomedial nucleus is probably more related to disruption of the frontal network than to disruption of the medial temporal network.

It could be argued that part of the amnesia in our patient was caused by thalamo–cingulate disconnection, as the anterior thalamic radiation contains fibres that connect the anterior nucleus of the thalamus with the anterior cingulate gyrus,

Table 1 Results of neuropsychological tests

Test	Full score	Patient's score	Normative data*
<i>Wechsler memory scale-revised</i>			
Logical memory I	50	9	22.0 (7.1)
Logical memory II	50	0	16.8 (7.0)
Verbal paired associates I	24	7	16.7 (3.8)
Verbal paired associates II	24	2	7.0 (1.2)
Visual paired associates I	18	2	12.2 (4.0)
Visual paired associates II	18	0	5.0 (1.3)
Visual reproduction I	41	15	36.6 (5.0)
Visual reproduction II	41	0	33.1 (6.4)
Index for attention concentration	–	83	–
<i>Rey auditory verbal learning test</i>			
Total	75	23	41.6 (6.5)†
1/2/3/4/5	15 each	4/4/5/6/4	–
Recognition	15	11	13.0 (1.3)†
<i>Rey-Osterrieth complex figure</i>			
Copy	36	31	16th centile
Immediate recall	36	2	1st centile
Recognition	24	18	10th centile
<i>Benton visual retention (type A)</i>			
Correct	10	4	7.0 (1.3)
Error	0	17	3.9 (1.9)
<i>Autobiographical memory interview</i>			
Autobiographical episodes			
Childhood	9	9	(acceptable range)
Early adult life	9	7	(acceptable range)
Recent life	9	5	(definitely abnormal)
Autobiographical semantics			
Childhood	21	20	(acceptable range)
Early adult life	21	17	(acceptable range)
Recent life	21	13	(definitely abnormal)
<i>Wisconsin card sorting test</i>			
Categories	6	1	6–10th centile
Perseverative errors	0	90.1	1st centile
<i>Trail making test</i>			
A	–	71 s	38 (12) s‡
B	–	173 s	88 (18) s‡
<i>Verbal fluency§</i>		21	33 (9.9)‡

*Normative data are presented as centiles for the Rey-Osterrieth complex figure test and the Wisconsin card sorting test, and as mean (SD) for the others. Evaluation provided by the publisher for the autobiographical memory interview.

†Age and education matched control (n=5).

‡Age and education matched control (n=7).

§Verbal fluency is presented as the sum of words produced in one minute, each of which begins with Japanese syllables "A", "Fu", and "Ni".

which is part of the Papez circuit. However, no clinical case with long standing amnesia has been reported with lesions in the anterior cingulate gyrus, although transient memory disturbance was observed after bilateral cingulectomy.²¹ Moreover, anterior cingulate lesions in monkeys do not cause significant impairment of the scene memory task, while performance of this task is impaired by lesions in the hippocampo-fornico-mammillo-thalamic system (the Delay-Brion system),^{22,23} and by lesions in the dorsomedial nucleus.¹⁷ Therefore, it is difficult to link the anterior limb lesion in our case with thalamo-cingulate disconnection.

Conclusions

Accumulating evidence indicates that memory is based on distributed networks, and lesions in any part of these networks can cause amnesia when the damage occurs bilaterally. Our case clearly shows that discrete lesions that are situated asymmetrically but strategically in the bilateral thalamo-frontal networks cause a definite amnesia. This type of amnesia should be carefully distinguished from amnesia caused by lesions in the Delay-Brion system.

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Competing interests: none declared

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Received 16 April 2002

In revised form 30 August 2002

Accepted 30 August 2002

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