Short report

Long-term cognitive recovery following isolated bilateral infarction of the fornix presenting with amnesia

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ABSTRACT

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Dr Jennifer Bradshaw; jennifer.bradshaw@austin. org.au **Introduction** Isolated infarction of the fornix is a relatively rare stroke syndrome frequently associated with amnesia. The long-term cognitive outcome in cases of acute fornix infarction is poorly understood. This is largely due to the limited number of case studies that have documented cognitive outcomes beyond the acute recovery phase on quantifiable neuropsychological measures. We describe a patient who developed acute amnesia and was subsequently diagnosed on cerebral MRI with bilateral infarction in the anterior columns of the fornix.

Method Comprehensive neuropsychological review was undertaken prospectively at baseline, early and late phases of recovery.

Results At 9 months post-stroke, there was some reduction in the severity of memory dysfunction, but a significant anterograde amnesia persisted.

Conclusion This is one of the very few cases in the literature where neuropsychological function has been comprehensively and serially examined over the first year post-isolated bilateral fornix infarction. It is concluded that amnesia can persist well beyond 6 months in these cases, with associated functional impairment in daily life.

INTRODUCTION

Infarction of the fornix is a relatively rare, but well documented, stroke syndrome involving the subcallosal artery or lateral posterior choroidal arteries.¹⁻⁴ The fornix plays a central role in human memory, as the major white matter outflow tract from the hippocampus. Previous case reports describe acute amnesia as the main presenting symptom of fornix infarction and there is clinical and experimental data to suggest a functional distribution of the forniceal fibres.⁵ Both anterograde and retrograde amnesia are possible, with case studies suggesting an increased incidence of anterograde memory impairment associated with lesions of the fornix.⁶⁻¹⁰

Clinical recovery following fornix infarction is less well understood.¹¹ Memory symptoms may be, in part, reversible and the expected recovery time frame varies from weeks to months.¹ Persistent and significant memory dysfunction has also been reported in some cases.⁶ ¹² This variability in clinical outcome might be explained by the incomplete involvement of the forniceal structures and associated ischaemia of nearby structures that subserve memory. Others have criticised the lack of comprehensive psychometric data necessary to document the true nature and extent of any residual memory dysfunction following isolated infarction of the fornix.⁶⁹¹²

To our knowledge, there are only five other case reports with detailed neuropsychological follow-up following relatively focal infarc-tion of the fornix^{6 7 9 13 14} and only one was followed up beyond 6 months post stroke.⁶ Comprehensive, long-term neuropsychological studies are lacking and would greatly improve our understanding of the expected recovery time frames and cognitive outcomes after fornix infarction. This is particularly relevant for clinicians attempting to provide prognostic information to young stroke patients, where the integrity of memory function is central to their ability to return to independent living. We describe the findings from serial neuropsychological review undertaken in a young patient with an isolated ischaemic infarction of the fornix.

Case history

A patient in their 30s presented with 48 hours of 'confusion and disorientation'. This was characterised by a sudden inability to recall details of recent events and conversations while travelling with family on holiday. The partner noted that the patient was forgetful of their daily travel itinerary and could not recall recent food and drink purchases or their location. They were able to reliably recall biographical information preceding the onset of confusion and remained oriented to the year and month but could not recall the date or day of the week. There was no disturbance of conscious state or fluctuation in attention, nor was there any language disturbance, psychotic phenomena, or personality change.



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Figure 1 (A) Axial MR diffusion weighted imaging (DWI) and (B) corresponding apparent diffusion coefficient (ADC) showing acute bilateral infarction in the anterior columns of the fornix.

The patient did not experience headache, fever or any witnessed seizure activity and there was no history of head trauma. Alcohol intake was relatively increased while on holiday with four standard drinks being consumed in the 24 hours preceding presentation. However, there was no prior history of consistent heavy alcohol consumption. Previous medical history was only significant for well-controlled ulcerative colitis. The patient was a nonsmoker and had no known cardiovascular risk factors. The Moderna COVID vaccine had been administered 4weeks prior, but the patient had remained systemically well and had no symptoms or signs of other illness.

Neurological examination at the local hospital emergency department was unrevealing except for persisting anterograde amnesia and abnormal cerebral MRI. MRI (day 3; figure 1) documented bilateral symmetrical foci of diffusion restriction and fluid attenuated inversion recovery hyperintensity lateral to the foramen of Monro. The patient was then transferred to an acute stroke unit at a major public hospital and diagnosed with bilateral fornix infarction (day 5). Despite this finding, the formal National Institutes of Health Stroke Score on transfer was 0. Aspirin (100 mg) per day and atorvastatin (80 mg) per day were commenced as secondary stroke prevention. A full young stroke screen was performed with no underlying thrombophilia or diabetes being identified. New dyslipidaemia was diagnosed and a patent foramen ovale was found as a suspected stroke mechanism.

Neuropsychological examination at baseline (day 10)

The patient was alert and oriented to the year and month, but not the date or day of the week. There was no spontaneous report of memory difficulties, giving an impression of limited insight. On specific questioning, the patient could not reliably recall details of recent events. No repetitiveness was noted in conversation, nor was there evidence of confabulation. Formal examination (table 1) revealed mild reductions in attentional processing and a severe anterograde memory deficit for both verbal and visuospatial materials.

There were notable deficits in delayed recall, characterised by an inability to learn and retain novel word lists, visual images and arbitrarily associated information. Recall was not reliably assisted by recognition cues, with a high rate of false-positive responding. Spatio-constructional function was intact. Conversational speech and language were also unremarkable, although performances on measures of confrontation naming and strategic lexical retrieval were mildly reduced relative to normative expectations. Fronto-executive functions were well preserved.

Neuropsychological examination at early and late phases of recovery

Four weeks

At 1-month post stroke, the patient was better oriented to time, more certain of the year and only 1 day out on the correct day/date but remained unaware of ongoing ට

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Continued

Table 1 Continued

Neuropsychological test	Time interva				
	10 days	4 weeks	4 months	9 months	Normative data
Easy pairs (max 18)	12	18		17	
Hard pairs (max 12)	0	5		6	
AL score (max 21)	6	14		14.5	18.21±2.28
Long delay					
Easy pairs (max 6)	5	6		6	
Hard pairs (max 4)	0	1		2	
AL score (max 10)	5	7		8	9.92±0.28
RCFT					
Short delay (max 36)	7	14		13	18.9±6.10
Long delay (max 36)	3	14		12	19.50±6.70

AL, Associate Learning; ASS, Age Scaled Score; BNT, Boston Naming Test; COWAT, Controlled Oral Word Association Test; CVLT-3, California Verbal Learning Test - Third Edition; C/W, Colour/Word; FSIQ, Full Scale IQ; LM, Logical Memory; PRI, Perceptual Reasoning Index; PSI, Processing Speed Index; RCFT, Rey Complex Figure Test; TMT, Trail Making Test; VCI, Verbal Comprehension Index; VR, Visual Reproduction; WAIS-IV, Wechsler Adult Intelligence Scale—Fourth Edition; WMI, Working Memory Index; WMS-IV, Wechsler Memory Scale -Fourth Edition.

memory limitations, except when confronted by memory failures. Collateral history highlighted persisting daily forgetfulness, including inability to recall details of recent conversations and forthcoming events, and the location of personal belongings. The patient was also heavily reliant on a mobile phone to keep track of the day and date.

Objective examination (table 1) revealed evidence of improvement in learning efficiency, consistent with the observed improvement on measures of attentional function. A relatively isolated and moderately severe anterograde memory deficit persisted for both verbal and visuospatial material. Mild improvement was seen in arbitrary associative learning, but this remained moderately impaired. Recognition recall remained unreliable. Previous reductions in confrontation naming and strategic lexical retrieval had resolved, and broader cognitive functions remained well preserved.

Four months

Four months into the recovery, the patient remained only partially oriented to time (incorrectly reported the day and date), but attentional function and processing speed had recovered, as expected (table 1). This was accompanied by significant improvement in learning efficiency, but there was persisting moderate-to-severe impairment in delayed recall on verbal and non-verbal memory measures, which was not reliably assisted by prompts or recognition cues. Intellectual performances fell in the 'average' to 'high average' range. Broader cognitive function was intact.

Nine months

At 9 months post stroke, family reported ongoing daily forgetfulness, with heavy reliance on compensatory strategies to support memory (eg, written reminders, diary use, phone alarms). The patient was cleared to return to driving but was not able to return to their previous work role, due to residual memory difficulties. On objective examination, orientation was now intact to person, place and time. Arbitrary associative learning and delayed recall showed mild improvement compared with the previous examination 5 months earlier, but delayed recall was not reliably assisted by recognition cues (table 1). These encouraging signs of memory recovery suggested reduction in the severity of memory dysfunction over the year, but the persisting mild-to-moderate anterograde memory disorder required ongoing use of compensatory memory strategies in daily life.

DISCUSSION

The expected recovery time frame and likely prognosis for long-term cognitive outcome in cases of acute fornix infarction are poorly understood. This is largely due to the rarity of the condition, combined with the limited number of case studies that have documented longer term recovery on quantifiable neuropsychological measures.

Our young adult patient had no known cerebrovascular risk factors and no pre-existing neurological disability or cognitive impairment. There were mild attentional and language deficits observed in the acute recovery phase that resolved by 4 weeks post stroke, but a significant anterograde memory deficit persisted.

Serial neuropsychological examination showed longer term improvement in memory function over 9 months post stroke. This is consistent with the only comparable case study, by Kauppila and colleagues.⁶. In their case, there was a sustained mild anterograde memory deficit, similar to the current case where memory function had not returned to normal by 9 months, with ongoing objective impairment in anterograde memory that significantly impacted quality of life.

In the few cases of focal fornix infarction with longer term, detailed neuropsychological examination, the available psychometric data suggest that these patients experience an isolated anterograde amnesia that persists for more than 6 months, and up to 9 months in our case. Severity of memory dysfunction does appear to improve over weeks to months, but in our young patient remained disabling with a significant impact on return-to-work capacity.

Finally, it should be noted that as the focus of this case study was on recovery of cognitive function, memory function in particular, less time was afforded to systematic exploration of other aspects of recovery (eg, functional abilities and mood), which is a potential limitation of this report.

Conclusion

The long-term course of cognitive recovery after acute fornix infarction is uncertain due to a paucity of detailed neuropsychological follow-up beyond the acute recovery phase. We describe the neuropsychological profile and pattern of recovery in a case of acute bilateral fornix infarction presenting with sudden onset amnesia. This is one of the few cases where neuropsychological functioning has been comprehensively and serially examined over the first-year post stroke. We conclude that significant impairment of memory can persist at 9 months post bilateral fornix infarction with associated functional impairment in daily life.

Contributors JB conceived the original idea and wrote the manuscript with support from PC and SW. We fully acknowledge the contribution of our patient and their family to the development of our knowledge in this area. We also acknowledge the contribution of the patient's rehabilitation specialists and their knowledge regarding the patient's progress in the later stages of recovery.

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Data availability statement All data relevant to the study are included in the article.

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