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Amnestic Syndrome Following Surgical Transection of Fornix: A Single Case Study with Short-Term Follow-up

Streszczenie

Artykuł opisuje przypadek 25-letniej kobiety, u której wystąpił ciężki zespół amnestyczny po operacji torbieli koloidowej trzeciej komory mózgu. Pooperacyjne badanie radiologiczne ujawniło obustronne przecięcie sklepienia – wiązki włókien łączących struktury limbiczne zaangażowane w procesy pamięci. Wstępna, szczegółowa ocena neuropsychologiczna wykazała obecność niepamięci następczej jako izolowanego zaburzenia poznawczego. Chora uczestniczyła w programie rehabilitacji, który obejmował indywidualne i grupowe sesje treningu poznawczego. Zaobserwowano znaczącą poprawę funkcjonalną w trakcie sześciu tygodni zdrowienia wspomaganego rehabilitacją poznawczą, jednak ilościowe miary w postaci wyników testowych nie w pełni ją odzwierciedlały. Niniejsza praca przyczynia się do wzmocnienia istniejących dowodów na kluczową rolę

sklepienia w procesach pamięciowych. Omówione zostały także praktyczne i teoretyczne problemy związane z oceną funkcjonalną w tego typu przypadkach klinicznych.

Słowa kluczowe

zespół amnestyczny, sklepienie, ocena neuropsychologiczna, rehabilitacja poznawcza

Abstract

We describe the case of a 25-year-old female, who developed severe amnesic syndrome following surgical removal of a third-ventricle colloid cyst. Postoperative radiological examination revealed bilateral transection of fornix – a bundle of fibers which connects limbic structures involved in memory. Extensive initial neuropsychological assessment revealed anterograde memory impairment as an isolated cognitive disorder. The rehabilitation program comprised both individual and group cognitive training sessions. Significant functional improvement was observed during six weeks of recovery supported by rehabilitation. However, these improvements were not fully reflected in the quantitative measures. The study contributes to the growing evidence regarding the crucial role of the fornix in memory. Practical and theoretical issues related to functional assessment are discussed.

Keywords

amnesic syndrome, fornix, neuropsychological assessment, cognitive rehabilitation

Introduction

Amnesic syndrome is classically defined as profound, global (i.e., independent of a to-be-learned stimulus modality), and relatively isolated memory impairment caused by brain injury (O'Connor & Verfaellie, 2002). Lesion location is traditionally used to distinguish three amnesic syndromes: bilateral medial temporal lobe amnesia, diencephalic amnesia, and basal forebrain amnesia. Growing evidence suggests that these syndromes share many clinical characteristics on a behavioral level (Markowitsch & Staniloiu, 2013), with some questions raised regarding the differentiation of temporal lobe amnesia versus diencephalic amnesia. New data indicate that these two allegedly different syndromes should be considered disturbances of the “extended hippocampal system” (Aggleton & Brown, 1999) which encompasses hippocampi, mammillary bodies, anterior thalamic nuclei, and fornices. Focal damage to one element of this hippocampal–anterior thalamic axis appears sufficient to cause full-blown amnesic syndrome. The fact that structural damage in one site may cause functional (Caulo et al., 2005) and structural (Loftus, Knight & Amaral, 2000; Tsivilis et al., 2008) abnormalities in distal but connected structures in the neural memory system demonstrates the regulation of memory and human cognition in general by extended and complex cortico–subcortical networks.

Recent decades have seen the generation of considerable data regarding the role of fornix damage in amnesic syndrome. Such inquiry is prompted by the fact that fornices contain efferents from hippocampi to mammillary bodies and cholinergic afferents to hippocampi (Douet & Chang, 2015; Aggleton & Brown, 1999). Most related reports in humans concern the outcomes of surgical removal of a third-ventricle colloid cyst – a rare benign intracranial tumor. However, post-stroke bilateral damage to fornix has also been reported (Takano, Tatewaki, Mutoh, Ohara, Yamamoto, & Taki, 2018). The frequency of memory disorders after a surgical intervention varies considerably across studies (e.g., Mathiesen, Grane, Lindgren & Lindquist, 1997; Hernesniemi & Leivo, 1996; Desai, Nadkarni, Muzumdar & Goel, 2002). Such reports usually lack precise neuropsychological data. However, when a detailed neuropsychological assessment

is reported, a straightforward image emerges. A fornix transection – particularly bilateral and usually with a transcallosal surgical approach (Brandling-Bennett et al., 2012; Hernesniemi & Leivo, 1996) – leads to an amnesic syndrome (Aggleton et al., 2000; Calabrese, Markowitsch, Harders, Scholz, & Gehlen, 1995; Gaffan & Gaffan, 1991; Hodges & Carpenter, 1991; McMackin, Cockburn, Anslow & Gaffan 1995; Poreh et al., 2006; Vann et al., 2009; Mazarakis, Summers, Murray, Waiter, & Fouyas, 2011). Similar findings are reported regarding fornix damage resulting from isolated stroke (Korematsu, Hori, Morioka & Kuratsu, 2010) and TBI (D’Esposito, Verfaellie, Alexander & Katz, 1995).

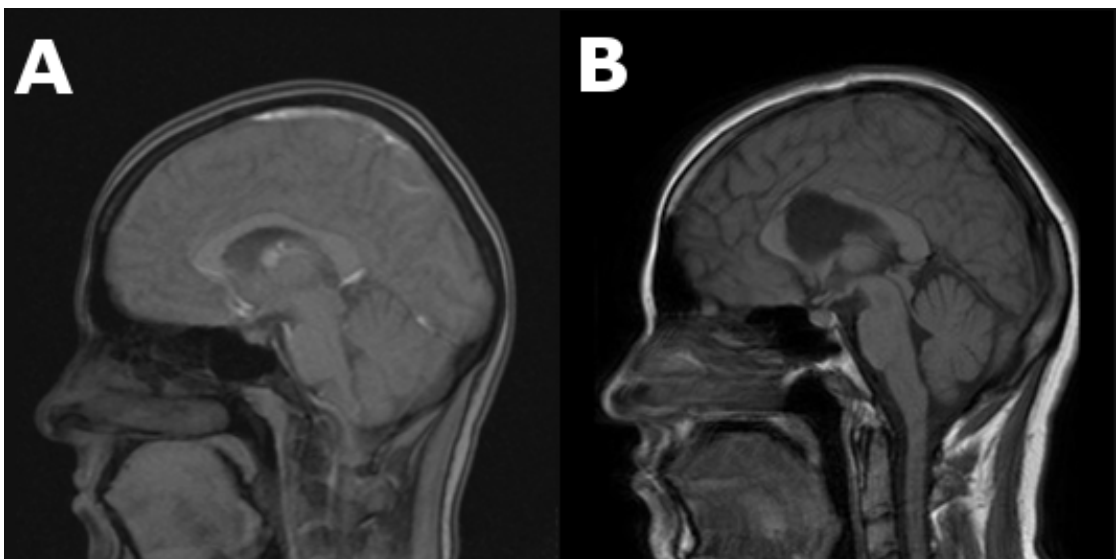
The present case study reports the neuropsychological profile of a young female patient who underwent third-ventricle colloid cyst removal. Extended neuropsychological assessment of memory and other cognitive domains was performed, using conventional cognitive tests, the ecologically valid tool – the Rivermead Behavioral Memory Test (Wilson et al., 2008; for a review of the issue of ecological test validity see: Marcotte, Scott, Kamat & Heaton, 2010) and observational, functional scales. These tools cover all disability levels distinguished by WHO (2001), i.e. impairment (conventional tests), activity limitations (ecological tests) and participation restrictions (functional scales). Follow-up neuropsychological examination was conducted after six weeks of rehabilitation in order to measure its effectiveness and the rate of recovery.

Materials and Methods

Case Report

A 25-year-old, right-handed female M.C., with 16 years of education was referred to the Department of Neurological Rehabilitation one month after surgical removal of a third-ventricle colloid cyst. The predominant symptoms on admission were severe amnesia and ataxia. Prior to surgery, the patient had been self-dependent in activities of daily living, without any cognitive or physical dysfunctions. During the approximately two-week period preceding surgery, the patient complained of headache, dizziness, nausea, vertigo, and photophobia. A brain tumor of $5 \times 7 \times 8$ mm in size was revealed by pre-surgical MRI (Figure 1A), and its exact type was confirmed by post-surgical histopathological examination.

Figure 1. The presurgical (A) and postsurgical (B)MRI of patient M.C. in sagittal view



Postsurgical MRI revealed lesions encompassing the genu, the anterior parts of the corpus callosum body and the cingulate cortex, and the fornix body (Figure 1B), typical sequelae of a transcallosal surgical approach.

Procedure

Neuropsychological Assessment

Neuropsychological examination performed four weeks after the surgery, involved detailed interviews with the patient and her relatives, observation of spontaneous behaviors during the patient's stay in the ward, and cognitive assessment with particular regard to memory functions. The following memory measures were included:

- Rey Auditory–Verbal Learning Test (RAVLT; Strauss, Sherman & Spreen, 2006) to measure learning, recollection, and recognition of verbal information;
- Rey Complex Figure Test (RCFT; Meyers & Meyers, 1995) to measure visuospatial memory;
- Rivermead Behavioral Memory Test (RBMT; Wilson et al., 2008), an ecologically valid battery for measuring various memory functions;
- Pattern Recognition Memory Test from Cambridge Neuropsychological Test Automated Battery (CANTAB, Cambridge Cognition, Cambridge, United Kingdom), a forced-choice visual recognition task with immediate and delayed trials;
- Boston Naming Test (BNT; Kaplan, Goodglass & Weintraub, 2000) to assess language functions, especially related to semantic memory;
- Information subtest of the WAIS-R (Brzezinski et al., 2004) to assess semantic memory;
- Vocabulary subtest of the WAIS-R, an indirect index of premorbid cognitive status (Lezak, Howieson & Loring, 2012);
- Mayo-Portland Adaptability Inventory 4 (MPAI-4; Malec & Lezak, 2008) and Functional Independence Measure/Functional Assessment Measure (FIM+FAM; Turner-Stokes, Nyein, Turner-Stokes, Gatehouse, 1999), both observation-based functional scales, with the items related to memory used alone to avoid confounding with other cognitive abilities. The assessment was conducted by the leading clinician (P. M.).

We also utilized the following short-term/working memory, attention, and executive functions tests:

- Digit Span Forward, Digit Span Backward (from WAIS-R) and Spatial Span Forward, Spatial Span Backward (SSP; from the computerized test battery CANTAB), respectively, to measure verbal and visuospatial aspects of working memory/attention;
- Rapid Visual Processing – the processing speed/attentional task from CANTAB;
- Delayed Matching to Sample task (DMS; from CANTAB), a computerized version of the forced-choice visual recognition task;
- Wisconsin Card-Sorting Test (WCST in the polish adaptation; Jaworowska, 2002) to assess abstract thinking and set-shifting functions of the executive system;
- Stockings of Cambridge (SOC), a computerized analogue of Tower of London from CANTAB battery, for testing complex task planning and execution;
- Similarities subtest of the WAIS-R, assessing abstract thinking;
- Raven's Progressive Matrices (RPM; Jaworowska & Szustrowa, 2000), a general fluid intelligence test.

We assumed that conventional cognitive tests, ecologically valid tests and functional scales served as indices of impairment, activity limitations and participation restrictions aspects of disability, respectively. Therefore, all levels of disability from the WHO framework (2001) were taken in consideration.

Neuropsychological Rehabilitation

Forty-minute individual training sessions were attended five days per week, and mainly comprised internal mnemonic strategy practice, for example, rehearsal with fixed and expanding schedules, organizing material, making associations, engaging multiple modalities in a learning process, loci method, and errorless learning. These interventions were supported by conventional memory training using the computerized battery for cognitive rehabilitation (RehaCom; Hasomed GmbH, Magdeburg, Germany). External strategies (e.g., based on digital devices and traditional calendars) were minimally practiced because the patient spontaneously used them to a great extent, with good functional results. The patient also participated in fifteen 60-minute group therapy sessions focused on education about post-injury memory problems and coping strategies (for detailed description, see Leśniak, Mazurkiewicz, Iwański, Szutkowska-Hoser & Seniów, 2018)

Results

Initial Neuropsychological Testing Results

Data from interview. The patient's main complaints (confirmed by family members) included severe problems remembering events, people and content of conversations. She seemed concerned and worried about being disoriented and helpless in many everyday situations showing no signs of anosognosia. However, her mood and affective reactions were appropriate to her status and complaints.

General intellectual functioning, attention/working memory, executive functions. Table 1 presents quantitative data regarding general intellectual functioning, attention/working memory, and executive functions. General fluid intelligence (RPM) was assessed as above average. The patient achieved an average score on Vocabulary subtest, suggesting good premorbid cognitive functioning. Immediate memory – usually considered as attentional span (Lezak, Howieson & Loring, 2012; see also Scott & Schoenberg, 2010) – was assessed in auditory (Digit Span forward) and visual modalities (SSP forward), and both scores were in the normal range. Normal scores were also achieved on the backward versions of both tasks, which are indicators of the executive working memory. Processing speed performance (RVP) was impaired in the first pre-treatment testing. However, RVP has a memory component and thus should not be treated as a simple measure of attention. The executive tests scores relating to planning ability (SOC), concept formation, and set shifting (WCST) were in the normal range. Abstract thinking was preserved (Similarities subtest). We concluded that executive/attentional functioning and general/fluid intelligence were rather spared. The cognitive measures that were assessed as normal in the pre-treatment testing were excluded from the follow-up.

Table 1. *The Patient's Scores and Their Normative Interpretations*

Neuropsychological test	Time of testing			
	Initial assessment		Follow-up	
	%	Interpretation	%	Interpretation
Raven's Progressive Matrices	85	High average	-	
WAIS-R				
Vocabulary	63	Average	-	
Information	50	Average	-	

	Time of testing			
	Initial assessment		Follow-up	
Similarities	75	High average	-	
Digit span	75	High average	-	
CANTAB				
Spatial span	50 (5a)	Average	50 (5a)	Average
Delayed matching to sample				
Delayed	0	Extremely low	0	Extremely low
Simultaneous	100	Very superior	100	Very superior
Pattern recognition memory				
Immediately	<5	Unusually low	<5	Unusually low
20-min delay	<5	Unusually low	<5	Unusually low
Stockings of Cambridge	60	Average	-	
Rapid visual processing	<1	Extremely low	<10*	Low average
WCST				
Perseverative errors	81	High average	-	
Categories	>16	Normal	-	
RAVLT				
A1 trial	6a		4a	
A5 trial	9a		8a	
A1-A5 sum	43a		32a	
Post-interference	0a		0a	
20-min delay	0a		0a	
Recognition	5a		3a	
RCFT				
Copy	99	Very superior	99	Very superior
3-min delay	<1 (10a)	Extremely low	31 (22a)b *	Average
30-min delay	<1 (0a)	Extremely low	24 (21a)b *	Low average
RBMT				
General memory index	<1	Extremely low	<1	Extremely low
First and second names (delayed)	2	Extremely low	5b	Unusually low
Belongings (prospective memory)	<1	Extremely low	<1	Extremely low
Appointments (prospective memory)	1	Extremely low	1	Extremely low
Picture recognition (delayed)	<1	Extremely low	<1	Extremely low
Story (prose recall)				
Immediate recall	25	Average	1	Extremely low
Delayed recall	<1	Extremely low	<1	Extremely low
Face recognition (delayed)	<1	Extremely low	<1	Extremely low
Route				
Immediate	<1	Extremely low	16*	Low average
Delayed	<1	Extremely low	5b	Unusually low
Messages (prospective memory)				
Immediate	16	Low average	50*	Average
Delayed	9	Low average	<1	Extremely low
Orientation and date	<1	Extremely low	<1	Extremely low

	Time of testing			
	Initial assessment		Follow-up	
Novel task				
Immediate	2	Unusually low	25*	Average
Delayed	9	Low average	<1 ^b	Extremely low
FIM/FAM – the memory item	1c – total assistance, i.e., subject contributes <25% of the effort or is unable to do the task		3c – moderate assistance, i.e., subject still performs 50-75% of the task	
MPAI-4				
Memory item (“Problems learning and recalling new information”)	4c,d – severe problems; interferences with activities more than 75% of the time		3c,d – moderate problem; interferences with activities 25-75% of the time	
Fund of information item (“Problems remembering information learned in school or on the job; difficulty remembering information about self and family from years ago”)	1c,d – mild problem		1c,d – mild problem	

Note. The obtained scores were converted to the percentile scale (see Strauss, Sherman & Spreen, 2006). When informative, raw scores were also reported. The Wechsler system of classification ranges was derived from Brooks, Sherman, Iverson, Slick & Strauss (2011). CANTAB, Cambridge Neuropsychological Test Automated Battery; FIM/FAM, Functional Independence Measure/Functional Assessment Measure; MPAI-4, Mayo-Portland Adaptability Inventory 4; RAVLT, Rey Auditory Verbal Learning Test; RBMT, Rivermead Behavioural Memory Test; RCFT, Rey Complex Figure Test; WCST, Wisconsin Card Sorting Test; WAIS-R, Wechsler Adult Intelligence Scale – Revised.

*Improvement of >1 SD.

^aRaw score.

^bImprovement related to remembering an immediate memory test trial after a delayed trial completion.

^cLikert-type scale.

^dDetailed qualitative description of the Likert-type scale available in Malec & Lezak (2008).

Memory functions. Table 1 presents scores on the specific memory function measures. Verbal memory (RAVLT) was severely impaired. Immediate memory span (A1) could be considered normal. Introduction of the distractor list of words prevented the patient from recalling any information from the previously read list. After a 20-minute delay, recall and recognition were severely impaired such that the patient did not remember that the examiner had read the word list. RCFT scores revealed clear pathology in visuospatial memory. The three-minute delay figure reproduction was significantly incomplete, in striking contradiction to the maximum direct copy score. After the next 27-minute delay, the patient could not freely recall anything about the prior figure copying.

Visuospatial recognition memory scores (PRM, DMS) were also well below normal. Although these are roughly immediate tests, some characteristics of PRM (interference due to sequential presentation of a supraspan and the presentation pace during a forced-choice phase) and DMS (a delay) may make them difficult for amnesic patients. The patient also performed poorly on the ecologically valid RBMT. The overall score fell considerably below the normal range. Considering the particular subtests of RBMT, the vast majority of scores were in the range suggesting pathology. The exceptions were the subtests measuring immediate verbal prose memory and short-term prospective memory, where normal scores were obtained, which is consistent with the above-mentioned verbal test (immediate span in RAVLT). After delay the patient usually had no recollection of the immediate memory tasks.

Furthermore, when asked about the date the patient usually stated the approximate date of the surgery, which is in line with the predominantly anterograde amnesia. Analysis of this case provided cogent evidence for the high fragility of stored memory traces when faced with interference, and for severely impaired consolidation in the described type of amnesia. The quantitative and qualitative data strongly supported the diagnosis of severe anterograde amnesia. Retrograde memory was assessed by means of interview pertaining mainly to the events suggested by Kopelman and colleagues (1989). Retrograde amnesia with a marked temporal gradient was observed. Memories from childhood were relatively spared in contrast with moderate deficit regarding adolescence and early adulthood, and severe deficits regarding events that had occurred during approximately 6 months prior to the surgical intervention. Some difficulties with naming were observed in everyday situations and in the chosen items of BNT, but her speech was fluent.

Follow-up Assessment Results

Follow-up testing after approximately six weeks of rehabilitation did not show significantly changed quantitative scores, with the exceptions of relatively better performance on the immediate and delayed visuospatial memory tasks (RCFT and the three RBMT subtests). Worsening of the test scores was observed either. This may suggest the possibility of intermittent attentional problems. Nevertheless, overall daily functioning did substantially improve. The patient began to remember more information pertaining to the daily episodes from previous days, with improved quantities of remembered episodes and superior elaboration compared to in the pre-rehabilitation period. To quantitatively describe this functional improvement, we conducted retrospective assessment using the memory items from MPAI-4 and FIM+FAM. Both scales provided a sufficiently accurate scoring system to describe the functional behavioral change (Table 1). Despite the lack of considerable quantitative improvement on memory tests, the patient was able to remember her test performance after delays, which had been highly problematic before rehabilitation. This rather qualitative advancement in test performance was in agreement with the improved functioning in natural situations. Overall, the significant functional recovery (mainly related to everyday episodic/autobiographical memory) was weakly reflected in the tests scores (the majority of the post-interference and/or delayed trials remained in the impaired range).

Discussion

The presented case confirms that fornix damage can lead to profound amnesic syndrome with predominant anterograde and less severe retrograde memory disturbances. The use of the term “amnesic syndrome” is valid because of the multimodal and relatively isolated nature of these dysfunctions. The patient’s anterograde amnesia characteristics were congruent with other studies of amnesia with a similar brain injury location (Aggleton et al., 2000; Calabrese, Markowitsch, Harders, Scholz, & Gehlen, 1995; Hodges & Carpenter, 1991; McMackin, Cockburn, Anslow & Gaffan 1995; Poreh et al., 2006; Vann et al., 2009). However, retrograde amnesia is not always observed with such damage (Calabrese, Markowitsch, Harders, Scholz, & Gehlen, 1995; Hodges & Carpenter, 1991; but see Poreh et al., 2006), and therefore these cases should be elaborated with a focus on applied measurement tools, subject age, time from onset, and possible rapid withdrawal of symptoms (Hodges & Carpenter, 1991). Importantly, the presently observed memory disorder compromised both recall and recognition functions, which touches the theoretically sound distinction related to the functional and anatomical interdependence of these two memory processes (Aggleton & Brown, 1999; Kopelman et al., 2007; Rudebeck et al., 2009; Squire, Wixted & Clark, 2007; Tsivilis et al., 2008; Vann et al., 2009). Based on the literature, we considered the fornix transection as the paramount radiological finding and the cause of amnesia in our patient. The lesions of the cingulate cortex and the corpus callosum (as co-morbid injuries) probably had no direct impact on memory functions.

Based on the clinical observations of our patient and her scoring on the functional scales, we claim that some functional improvement in participation restrictions is possible in first months after a fornix transection, although it may not be fully revealed by quantitative psychometric evaluation of impairment and activity limitations. Most memory measures that showed better test performance concerned visuospatial memory function (RCFT and some RBMT subtests: immediate Route, immediate Message, and immediate Novel Task). Importantly, among the delayed trials, only RCFT was a sufficiently sensitive test to detect any change in memory. Hodges & Carpenter (1991) described a similar pattern of improvement – including superior RCFT scores at follow-up and good functional adaptation. However, cases with a similar type of amnesia and no improvement have also been reported (e.g., Poreh et al., 2006).

In our case study, improvement assessed by the functional scales MPAI-4 and FIM+FAM was rather weakly reflected by the change in the test scores, even using the ecologically valid tool. This fact raises questions regarding the actual ecological validity of RBMT, which is determined by two approaches: the degree to which the test items resemble everyday situations (i.e., verisimilitude) and the empirically examined strength of the relationship between the test scores and everyday functioning measures (i.e., veridicality). Considering both aspects, RBMT is reportedly superior to other conventional memory tests (Makatura, Lam, Leahy, Castillo, & Kalpakjian, 1999; see also: Chaytor & Schmitter-Edgecombe, 2003). The lack of relationship between the RBMT and functional scale scores in our patient may have been due to her excellent compensatory skills. Since standardized tests tend to preclude or minimize usage of compensatory strategies (especially external), this is a major factor that may weaken the link between these two kinds of measures (see Chaytor & Schmitter-Edgecombe, 2003).

The relative importance of spontaneous early recovery and of training-induced/guided recovery (Robertson & Murre, 1999) cannot be addressed based on this single case report. The exact mechanism of partial functional recovery itself is probably multifactorial and difficult to unambiguously identify. Potential explanations could include the functional re-enactment of spared redundant tracts within the neural memory network (Mazarakis, Summers, Murray, Waiter, & Fouyas, 2011) and/or the beneficial effect of the patient's compensatory behaviors.

Conclusions and Future Prospects

The presented case unequivocally demonstrates that fornix damage may cause amnesic syndrome with predominant anterograde deficit. It also indicates that retrograde deficit is possible, whereas prior publications have reported mixed results concerning this symptom. Furthermore, our case study shows that conventional and ecologically valid tests may be insufficient to detect partial functional recovery in amnesic patients. Instead, this requires very careful observation of behavior in natural situations and its description on functional scales. This observational assessment should be made by a clinician, significant others, and the patient him/herself; disparities between such scores may also have informative value. It is also crucial to investigate the role of third variables, which can and supposedly usually do moderate or mediate the relationships between independent and dependent variables (Baron & Kenny, 1986) – here, treatments and outcomes, respectively. For example, we hypothesized that the disparity between formal test scores and functional assessment of improvement may be conditioned by intensive use of internal and/or external compensatory strategies in natural conditions. Finally, our findings support recommendations to avoid interventions that may result in cutting the fornical tracts during surgical removal of third-ventricle tumors whenever possible (Brandling-Bennett et al., 2012).

This study has several limitations. First, since the patient was assessed twice (with a six-week interval) alternate versions of cognitive tests could have been used to avoid practice effect. It is possible that previous exposure contributed to the observed minimal improvements in some memory tests despite patient's dense amnesia and her unawareness of being presented with the memory material. Another drawback is lack of quantitative data describing everyday memory functioning. FIM+FAM and MPAI-4 are rather crude measures of cognitive functioning. Future studies should use more detailed observational scales. ■

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STUDIUM Z NAMI

1. Najwyższy poziom naukowy i prestiż Uniwersytetu Wrocławskiego
2. Szeroka oferta zajęć podstawowych, fakultatywnych i specjalizacyjnych
3. Elastyczny plan zajęć
4. Rozwijanie zainteresowań w ramach laboratoriów i kół naukowych
5. Możliwość wyjazdów w ramach programu MOST lub Erasmus +
6. Praktyki w zakresie diagnozy i terapii
7. Dbłość o relację mistrz - uczeń
8. Konkurencyjne czesne dla studentów wieczorowych



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