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Case Report

Cognitive and functional outcomes following a traumatic brain injury sustained 22 years after epilepsy surgery: A case report

Julie K. Janecek [a,*], Jeffrey R. Binder [a], Wade M. Mueller [b], Sara J. Swanson [a]

[a] Department of Neurology, Medical College of Wisconsin, 8701 W. Watertown Plank Rd., Milwaukee, WI 53226, USA
[b] Department of Neurosurgery, Medical College of Wisconsin, 8701 W. Watertown Plank Rd., Milwaukee, WI 53226, USA

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ABSTRACT

Anterior temporal lobectomy (ATL) is an effective treatment for drug-resistant epilepsy, and risk for post-surgical naming and verbal memory decline after dominant hemisphere ATL is well-established. However, less is known about later life cognitive and functional outcomes following ATL performed in early or mid-life, as there are few studies that report very long-term outcomes, and the intersection of epilepsy and the aging process is not well-understood. Factors that may promote healthy cognitive aging or confer increased risk for cognitive decline in late life for those with seizure onset in early or mid-life have yet to be determined. This case report describes an individual with drug-resistant epilepsy who was treated with left ATL in mid-life, and then subsequently sustained a moderate traumatic brain injury 22 years later. The excellent recovery and remarkable stability of cognitive performance over time may be associated with several protective factors such as favorable seizure outcome, high cognitive reserve, and the absence of co-occurring medical conditions. This case also highlights the clinical utility of serial neuropsychological testing at multiple timepoints across the lifespan for those with epilepsy, and the importance of considering the clinical significance, or functional impact, of cognitive deficits in this population.

1. Introduction

Anterior temporal lobectomy (ATL) is an effective treatment for temporal lobe epilepsy [1], and the risk for language and verbal memory decline after dominant hemisphere ATL is well-established [2,3]. However, relatively little is known about cognitive function in late life following ATL that was performed in early or mid-life. As life expectancy increases and individuals with epilepsy are living longer, understanding the intersection between epilepsy and the aging process is of significant interest. Several trajectories of cognitive decline in epilepsy have been proposed. One model suggests cognition is poorer at baseline but otherwise parallels typical aging [4,5]. A "second hit" model proposes that epilepsy is one of two or more neurological insults; the first hit is associated with incomplete recovery and reduced functional reserve, followed by a cognitive trajectory that parallels typical aging until the second hit occurs, which causes a cascadic deterioration and accelerated cognitive decline [6]. Finally, a chronic accumulation model hypothesizes that accelerated cognitive decline may be related to the interactive effects of seizures, decreased cognitive and brain reserve, and co-morbid conditions that are common in older age [7].

Studies of very long-term outcomes after right or left temporal lobe resection have yielded mixed results. In several group studies of participants with an average age in the fifth decade of life and mean follow-up intervals of 8–12.8 years, accelerated cognitive decline was not demonstrated following ATL [8–11]. In some instances, progressive cognitive decline has been observed in a subset of individuals with epilepsy following ATL, such as females [9] those with poor seizure control [9–11] and those with higher 1-year post-surgical cognitive scores [2]. In a case series of six older adults with a mean age of 61 who underwent presurgical evaluations and follow-up evaluations with a mean interval of 18 years, two patients with left temporal resections who were seizure free showed verbal memory declines, while four patients (two with left temporal resections and two with right temporal resections) showed stable memory scores over time [12]. In a case study of an 82-year-old woman who was seen 56 years following left temporal resection with complete seizure freedom, the cognitive course was described as similar to peers with the exception of

* Corresponding author at: Division of Neuropsychology, Department of Neurology, Medical College of Wisconsin, 8701 W. Watertown Plank Rd., Milwaukee, WI 53226, USA.
E-mail addresses: jjanecek@mcw.edu (J.K. Janecek), jbinder@mcw.edu (J.R. Binder), wmueller@mcw.edu (W.M. Mueller), sswanson@mcw.edu (S.J. Swanson).

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verbal memory and language deficits, which worsened over time, but were not debilitating [13].

Traumatic brain injury (TBI) is a significant cause of disability that is often associated with cognitive impairment in the general population [14]. Cognitive recovery following TBI is highly variable and has been related to numerous biopsychosocial factors. After moderate or severe TBI, the trajectory of cognitive recovery is typically most accelerated during the first several months post-injury, with a lesser degree of continued recovery occurring over the following months to years [15]. Poorer cognitive outcomes have been associated with more severe primary or secondary injuries such as hemorrhage, neuroinflammation, diffuse axonal injury, hypoxia, increased intracranial pressure, and/or post-traumatic seizures, as well as co-morbid medical and/or psychiatric conditions, older age, and less cognitive reserve [16–18].

We report cognitive and functional outcomes for an individual with a history of drug-resistant epilepsy who underwent left ATL in mid-life and then sustained a moderate TBI in late life. This case highlights several potential protective factors that may be related to stable cognition across the lifespan, even in the context of multiple neurological insults. Moreover, this case emphasizes the need for careful consideration of the clinical significance of cognitive deficits that may be observed in this population. In the absence of baseline neuropsychological data, it can be difficult to ascertain whether weaknesses in a cognitive profile represent stability or recent declines, which has implications for recommendations and treatment planning for individuals who are status-post ATL. Therefore, this case supports the previously published recommendation for routine cognitive assessment in new onset epilepsy patients as a part of standard clinical practice [19].

2. Case report

2.1. Clinical history: epilepsy

The patient provided written informed consent giving permission to submit this data, which was collected as part of routine clinical care, for publication. A 42-year-old right-handed male with drug-resistant epilepsy was referred for surgical evaluation. He had a single febrile seizure at one year of age, a single focal to bilateral generalized tonic-clonic (FBTC) seizure associated with a tonsillectomy at age 4, and recurrent seizures beginning at age 20. Seizure types included focal aware events every other week, focal with impaired awareness events twice per year, and GTC events twice per year. Anti-epileptic drugs (AEDs) were phenytoin and divalproex prior to surgery, phenytoin and gabapentin at the 6-month post-surgical evaluation, and phenytoin at 22-year follow-up. He underwent left ATL at age 42 and subsequently had three seizures: one focal impaired awareness seizure 2 months post-operatively, one FBTC seizure 14 years post-operatively, and one FBTC seizure following a traumatic brain injury 22 years post-operatively.

2.1.1. Medical, psychiatric, and psychosocial history

There were no birth complications, and developmental milestones were met on time. Additional medical history is significant for melanoma. Psychiatric history is significant for generalized anxiety disorder and depressive disorder, unspecified. Medications at the time of his post-TBI evaluation included escitalopram, duloxetine, and phenytoin. Academically, he was an excellent student who earned bachelor's and master's degrees in business and engineering. He works full-time in a managerial role. He is married and has two children.

2.1.2. Pre-surgical evaluation

Video electroencephalogram showed a left temporal seizure focus. Magnetic resonance imaging (MRI) of the brain indicated left mesial temporal sclerosis. Functional MRI revealed left hemisphere language dominance using a semantic decision task [20]. Neurological exam was normal. Neuropsychological test results obtained approximately 4 months prior to surgery were largely average to above average except for weaknesses in picture naming, facial discrimination, and bimanual fine motor speed and dexterity (see Table 1).

2.1.3. Post-surgical evaluation

The patient underwent left ATL and returned for post-surgical neuropsychological evaluation approximately 8 months later. He had a single focal seizure with impaired awareness approximately 2 months following surgery (Engel Class IIB). Neuropsychological test results indicated improvement in facial discrimination and declines on measures of verbal and perceptual intellectual skills, wordlist learning and memory, and picture naming (see Table 1). Of note, these test findings indicate a dissociation between change in story learning and recall (no decline) and list learning and recall (significant decline) following left ATL. The list learning task, which contains semantically unrelated words, likely requires more effortful strategies to learn and recall items compared to a story memory task that contains contextually related information. This finding is consistent with previous literature that has shown semantically unrelated list learning and recall tasks are most sensitive to left temporal pathology and/or resection [21,22].

2.2. Clinical history: traumatic brain injury

At age 64, the patient sustained a moderate traumatic brain injury (TBI). He fell down a flight of stairs and briefly lost consciousness. Duration of post-traumatic amnesia was approximately two days. His initial Glasgow Coma Scale score was 11 but declined to 3 when he had a FBTC seizure. Acute CT of the head showed intraparenchymal hemorrhagic contusions in the left temporal lobe and bilateral anterior-inferior frontal lobes, scattered subarachnoid hemorrhage and small subdural hematomas with a small amount of intraventricular hemorrhage, and remote postsurgical changes with a large region of cystic encephalomalacia and subadjacent gliosis involving the anterior-inferior left temporal lobe. MRI of the brain showed bifrontal hemorrhagic contusions, a contusion within the right anterior temporal lobe, and scattered subarachnoid, intraventricular, and parenchymal based blood products (Fig. 1). He was admitted to the hospital for approximately one week and then transferred to inpatient rehabilitation for approximately one week, where routine physical therapy, occupational therapy, and speech therapy services were initiated, and then discharged to his home.

2.2.1. Post-TBI neuropsychological screening

Approximately 2 months post-TBI, he was referred for an evaluation in a multidisciplinary Traumatic Brain Injury Clinic staffed by providers from physical medicine and rehabilitation and neuropsychology to characterize his recovery following TBI and determine his readiness to return to work. At that time, he reported being nearly at his pre-injury baseline and was hoping to return to work soon. Brief neuropsychological testing revealed significant verbal memory impairment and milder weaknesses in auditory attention and verbal fluency (see Table 1), although the clinical significance of these finding was not entirely clear, given his history of left ATL. Given the nature of his job, which was associated with potential risk to the well-being of his community if errors were made, he was not cleared to return to work, and an additional

Table 1
Neuropsychological Test Data.

	Pre-Surgical 4 months pre-ATL 1997	Post-Surgical 8 months post-ATL 1997	Post-TBI Screening 2 months post-TBI 2019	Post-TBI Evaluation 3 months post-TBI 2019
Wechsler Adult Intelligence Scale	**WAIS-R**	**WAIS-R**	**WAIS-IV**	**WAIS-IV**
Full Scale Intelligence Quotient	(113)	(99)		
Verbal Intelligence Quotient	(113)	(101)		
Attention-Concentration Deviation Quotient	(108)	(111)		
Similarities	23 (110)	22 (105)		28 (105)
Block Design	44 (125)	37 (110)		52 (120)
Digit Span	16 (105)	14 (100)	19 (80)	22 (90)
Digit Symbol/Coding	48 (95)	54 (100)	51 (90)	50 (90)
Wechsler Memory Scale	**WMS-R**	**WMS-R**		**WMS-IV**
Logical Memory Immediate Recall	24 (97)	28 (103)		21 (90)
Logical Memory Delayed Recall	15 (90)	22 (100)		16 (90)
Visual Reproduction Immediate Recall	33 (99)	32 (96)		37 (105)
Visual Reproduction Delayed Recall	33 (109)	26 (89)		27 (105)
List Learning and Memory	**SRT**	**SRT**	**HVLT-R**	**SRT**
Total Recall			19 (66)	
Long Term Storage	49 (102)	13 (57)		34 (85)
Consistent Long-Term Retrieval	48 (116)	10 (82)		17 (84)
Delayed Recall	8	2	3 (<55)	2
Recognition Discrimination	23	18	7 (<55)	19
Boston Naming Test	52 (70)	44 (52)		45 (66)
Judgment of Line Orientation	28 (109)	25 (102)		31 (>116)
Facial Recognition	39 (79)	49 (116)		44 (97)
Controlled Oral Word Association Test	**Letters CFL**	**Letters CFL**	**Letters FAS**	**Letters CFL**
Letter Fluency	39 (103)	37 (98)	27 (76)	38 (101)
Trail Making Test A	27″ (91)	31″ (85)	29″ (96)	26″ (103)
Trail Making Test B	58″ (90)	61″ (90)	56″ (104)	59″ (104)
Grooved Pegboard Right Hand	118″ (55)	83″ (69)		92″ (78)
Grooved Pegboard Left Hand	105″ (68)	85″ (82)		85″ (90)

Note: Raw scores are reported followed by standard scores (mean of 100, standard deviation of 15) in parentheses.
ATL – Anterior temporal lobectomy; TBI – Traumatic brain injury; WAIS-R, Wechsler Adult Intelligence Scale – Revised; WAIS-IV, Wechsler Adult Intelligence Scale – 4th Edition; WMS-R, Wechsler Memory Scale – Revised; WMS-IV, Wechsler Memory Scale – 4th Edition; SRT, Selective Reminding Test; HVLT-R, Hopkins Verbal Learning Test – Revised.

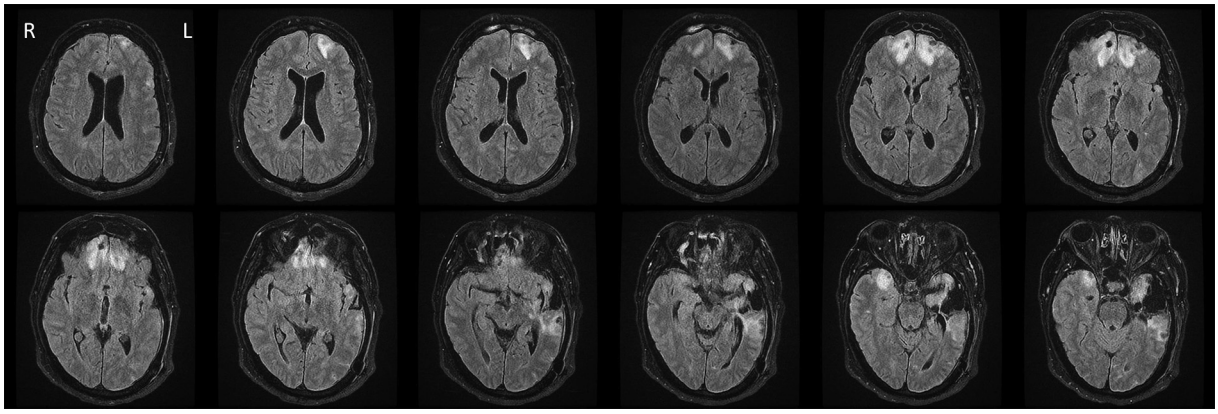

Fig. 1. MRI of the Brain Post-TBI. Note. Axial T2 FLAIR without contrast two days post-TBI.

month of recovery time followed by more comprehensive neuropsychological evaluation was recommended.

2.2.2. Post-TBI neuropsychological evaluation

Neuropsychological test results approximately 22 years following left ATL and 3 months following moderate TBI demonstrated excellent recovery and remarkable stability (i.e., no standard score changes greater than one standard deviation) relative to his 8-month post-ATL cognitive test scores (see Table 1 and Fig. 2). Although weaknesses were observed on measures of wordlist learning and memory and picture naming, these scores were unchanged compared to his 8-month post-ATL evaluation. Therefore, he was released to return to work part-time with oversight, with a plan to gradually increase his hours and responsibilities as tolerated. He subsequently successfully returned to work full-time and reportedly resumed his previous workload without difficulty.

3. Discussion

Despite a history of drug-resistant epilepsy, dominant hemisphere ATL, and moderate TBI, this patient demonstrated

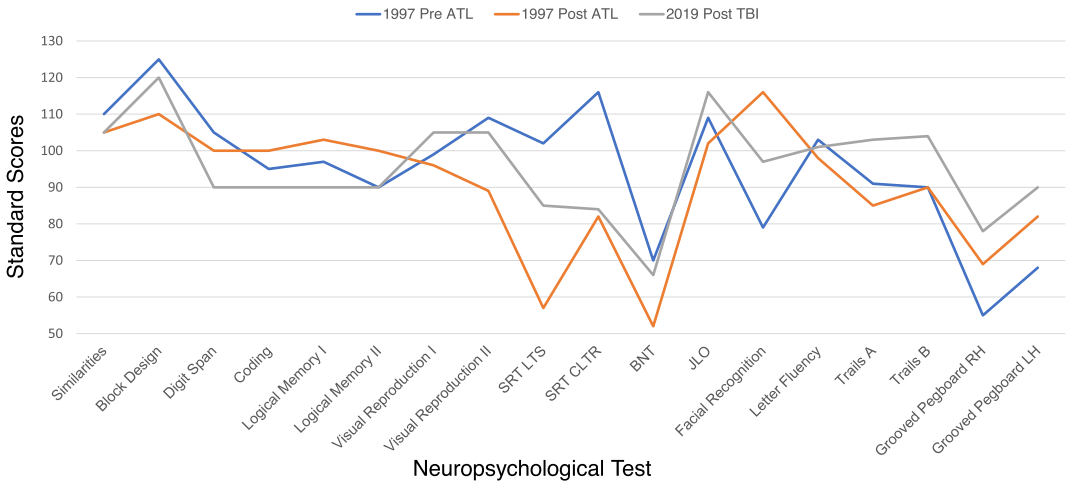

Fig. 2. Neuropsychological test performance. Note: Standard scores are reported for each test (mean of 100, standard deviation of 15), significance was defined as a change score of greater than or equal to 1 standard deviation and no post-ATL to post-TBI comparisons were significantly different. ATL – Anterior temporal lobectomy; TBI – Traumatic brain injury; SRT, Selective Reminding Test; LTS, Long Term Storage; CLTR, Consistent Long-Term Retrieval; BNT, Boston Naming Test; JLO, Judgment of Line Orientation; RH, right hand; LH, left hand.

remarkable cognitive stability over the course of 22 years. This case does not exemplify the proposed "second hit" model of accelerated cognitive decline [7]. Rather, it is consistent with several other reports that have not demonstrated accelerated cognitive decline following ATL in shorter follow-up durations [8,9,11] and a case report of very long-term follow-up [13]. There are several protective factors that may be associated with the good cognitive outcome in this case, including high cognitive reserve, good seizure outcome (two unprovoked seizures and one FBTC seizure following moderate TBI), and the absence of co-morbid medical conditions.

This case illustrates the potential challenges of interpreting neuropsychological data and making treatment recommendations in this population. When this individual initially underwent brief cognitive testing in the Traumatic Brain Injury Clinic, his previous medical records were unavailable. Understandably, concerns were raised by the treatment team about the possible degree of decline he may have experienced post-TBI and how this might impact his ability to return to work. However, the team did not want to restrict him from returning to his previous activities if he had in fact, returned to his pre-injury baseline. Without comparison cognitive test data from early or middle adulthood, we hypothesize that similar challenges related to data interpretation and treatment recommendations may occur with individuals who are post-ATL and are referred to memory care clinics in late life.

Finally, this case highlights the discrepancy that can exist between cognitive impairment and functional impairment in epilepsy. Individuals who experience cognitive decline post-ATL in early or mid-life may be able to compensate successfully. Although weaknesses in naming and verbal memory were observed in this patient, these findings were stable over time and reportedly did not negatively impact daily functioning earlier in life, which increased the medical team's confidence in releasing the patient to return to work. The patient has done well vocationally and returned to full-time employment in his previous occupation.

4. Conclusions

In summary, this case demonstrates remarkably stable and largely intact cognitive function across the lifespan in the context of drug-resistant epilepsy, left ATL performed at age 42, and moderate TBI sustained at age 64. Possible protective factors include high cognitive reserve, good seizure outcome, and absence of co-morbid medical conditions. This case depicts the clinical utility of serial clinical neuropsychological evaluations conducted at multiple timepoints across the lifespan for people with epilepsy and the possible dissociation between cognitive impairment and functional impairment. It also highlights the need for prospective longitudinal studies with very long follow-up intervals to investigate trajectories of cognitive function in epilepsy and to identify factors that are protective or increase risk for cognitive and functional decline in late life.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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