

Case Report

## Structural versus functional prediction of memory change following anterior temporal lobectomy

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### Abstract

Decline in recent memory function is a significant risk for patients undergoing anterior temporal lobectomy. We report a patient with a febrile seizure history, complex partial seizures arising from the left anterior temporal lobe, and MRI evidence suggesting left hippocampal sclerosis, all of which indicate a low likelihood of significant postoperative memory decline. However, high normal verbal memory on neuropsychological testing and bilaterally normal Wada memory scores indicated increased risk for postoperative memory decline. Following left anterior temporal lobectomy, the patient displayed a significant decline in verbal recent memory that affected school performance. Despite the worsening in memory, the patient reported a significant improvement in his self-reported quality-of-life perception, demonstrating that factors other than change in cognitive performance are related to whether a patient considers epilepsy surgery worthwhile. In the present case, behavioral measures were superior to structural measures in predicting cognitive change following surgery.

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### 1. Introduction

Risk of significant memory decline following anterior temporal lobectomy (ATL) remains an important concern, and valid assessment of this risk remains one of the goals of the preoperative evaluation. Prior to CT and later MRI, the primary concern was the development of a severe, persistent global amnesia, which could occur if the medial temporal lobe contralateral to the surgery was sufficiently dysfunctional that it could not support memory by itself [1].

To predict the presence of contralateral temporal lobe impairment, Milner et al. [2] introduced memory assessment during the period of hemispheric anesthesia associated with Wada testing. If patients could not adequately recall material following amobarbital injection

ipsilateral to seizure onset, significant contralateral medial temporal lobe disease was inferred and either patients were denied standard temporal lobe resection, or a more limited approach to surgery was taken. The incidence of amnesia has been extremely low after the introduction of Wada memory testing to the preoperative epilepsy surgery evaluation [3]. Although there have been reports of patients “passing” the Wada memory test and developing amnesia [4], complete details of these cases have never been formally presented.

Improvements in the diagnostic workup for surgery, including better invasive monitoring and functional imaging, have also contributed to the recognition of specific patients at risk for postoperative memory decline. Of all the developments, however, probably none is more significant than the capacity to image the hippocampi and medial temporal lobes with MRI [5]. Not only does MRI now play a critical role in the diagnostic workup and localization of seizure onset, the presence of MRI evidence suggesting hippocampal atrophy is

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associated with a favorable surgical outcome with respect to seizure frequency. The pathologic status of the resected temporal lobe is a critical factor associated with postoperative memory outcome [6,7], and patients who undergo resection of a relatively atrophic left hippocampus suggested by MRI are at decreased risk for postoperative memory decline [8]; patients with MRI evidence of bilateral hippocampal atrophy are at increased risk for postoperative memory decline following left ATL compared with those without evidence of contralateral hippocampal involvement [9,10].

Patients undergoing resection of the left language-dominant hemisphere are at greater risk for postoperative memory change compared with patients undergoing non-language-dominant resections [11], which likely reflects the importance of verbal memory in daily living activities. The degree of postoperative memory change is also related to preoperative performance levels; patients with better preoperative memory are at greater risk for a marked memory decline [11]. The absence of expected Wada memory asymmetries or good memory performance after contralateral injection is also associated with increased risk of significant verbal postoperative memory decline in patients undergoing left ATL [12,13].

In most patients, the different indices of postoperative memory risk are correlated, and even when they are not in complete agreement, they generally do not suggest incompatible outcomes. That is, one set of measures may suggest absence of risk whereas a different set produces inconclusive results. In the present report, however, we describe neuropsychological outcome in a patient with a history typical of the syndrome of medial temporal lobe epilepsy [14], including febrile seizures and MRI evidence of hippocampal sclerosis suggesting an absence of atypical risk for postoperative memory decline, but with behavioral data, including neuropsychological testing and Wada memory performance, in the above-average range, both of which suggest increased risk for postoperative memory decline.

## 2. Case report

At the time of surgical evaluation, the patient (E.G.) was a 21-year-old right-handed man who had dropped out of college due to increasing seizure frequency. E.G. was the product of an uncomplicated pregnancy and delivery, and met all developmental milestones on schedule. When he was 9 months of age, E.G. experienced a simple, uncomplicated febrile seizure. His habitual seizures began at age 15, although they were well controlled medically. He was an honors student in school and maintained a ‘B’ average. Following high school graduation, E.G. enrolled in a state university with a major in computer science. During his first semester at college, however, his seizures reemerged and,

although only occurring monthly, they were of sufficient psychosocial concern that he chose to drop out of school. Because his seizures could not be fully controlled despite multiple adjustments in his medical therapy, he subsequently underwent evaluation for epilepsy surgery. At the time of his epilepsy surgery evaluation, he was taking lamotrigine. Previous antiepileptic drugs (AEDs) included carbamazepine, gabapentin, phenobarbital, and valproate. MRI revealed left hippocampal atrophy consistent with medial temporal lobe sclerosis (see Fig. 1).

During his admission to the epilepsy unit for surgical evaluation, five complex partial seizures that did not generalize were recorded. All seizures started from the left anterior medial temporal lobe, with maximum EEG localization at SP<sub>1</sub> and T<sub>7</sub>.

### 2.1. Neuropsychological testing

Neuropsychological test scores are presented in Table 1. IQ scores were average to high average. His General Memory index on the Wechsler Memory Scale—III (WMS-III) was in the superior range, although he displayed significant material-specific asymmetry with “superior” delayed Auditory Memory and an “average”

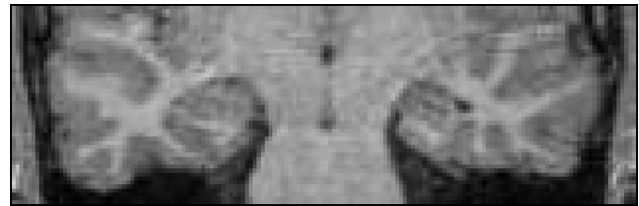


Fig. 1. MPRAGE image revealing left hippocampal atrophy.

Table 1  
Neuropsychological test results

Test	Preop	2 months	1 year
FSIQ	110	NA	115
VIQ	113	NA	115
PIQ	106	NA	113
Boston Naming	51	NA	48
COWA	25	NA	27
Semantic Fluency	30	NA	34
WMS-III General	120	117	117
Auditory Immediate	117	102	105
Auditory Delayed	124	108	108
Visual Immediate	103	115	115
Visual Delayed	100	115	122
Selective Reminding Test	SS = 112	SS = 67	SS = 72
CLTR			
SRT Delay	10/12	7/12	12/12
CF Copy	36	36	36
CF Immediate	27	25	34
CF Delay	29	29	34
QOLIE-89	47	NA	61

delayed Visual Memory index. Selective Reminding Continuous Long-Term Retrieval (CLTR) [15] indicated high normal verbal memory, and on Complex Figure [16], he demonstrated normal memory for complex designs. E.G.'s QOLIE-89 [17] score indicated an average quality-of-life perception.

Wada testing was performed using the MCG protocol [18], and E.G. was determined to be left cerebral language dominant. He obtained a recognition memory score of 8/8, with one false-positive recognition following left hemisphere injection of 100 mg and a recognition score of 8/8, with no false-positive recognitions following right hemisphere injection. During each injection, a contralateral hemiplegia was present during presentation of the memory stimuli.

### 2.2. Surgery

The patient underwent a left ATL with electrocortigraphy and stimulation mapping. The posterior resection margin along the superior and middle temporal gyrus was estimated to be 4.0 cm from the tip of the temporal lobe, and the posterior resection margin along the inferior temporal gyrus was estimated to be 5.5 cm.

### 2.3. Pathology

Pathology was reported in five temporal lobe specimens. The hippocampus was characterized by Ammon's horn sclerosis, marked white matter gliosis was present in the inferior temporal gyrus, the amygdala had moderate gliosis, marked subpial gliosis was present in the temporal polar cortex, and moderate subpial and white matter gliosis was described in the lateral temporal cortex.

### 2.4. Follow-up neuropsychological evaluation

Follow-up neuropsychological results are presented in Table 1. Because of concern for memory change and its effects on returning to school, a 2-month follow-up neuropsychological screening to assess memory was performed. E.G. complained of a noticeable decline in memory function which was corroborated by formal testing. Although his WMS-III General Memory index declined by only several points, his Delayed Auditory Memory index declined 16 points. This decline exceeds the 80% confidence interval for reliable change based on a longer average test-retest interval of 7.5 months [19]. The WMS-III decline was accompanied by a 30-point decline in Selective Reminding CLTR.

Standard neuropsychological evaluation was performed approximately 1 year following surgery. His WMS-III General Memory Delayed Auditory Memory index was unchanged from his 2-month follow-up assessment. Selective Reminding CLTR continued to be poor, with a CLTR score 27 points lower than present

preoperatively. Quality of life had improved 14 *T*-score points from his preoperative score, corresponding to a percentile change of 50 points.

### 3. Discussion

The likelihood of developing significant memory impairment following temporal lobectomy is one of the factors in the evaluation for surgical candidacy. Consequently, prediction of postoperative memory function remains one of the primary goals in the preoperative evaluation for epilepsy surgery. The factors that are generally considered in evaluation of risk to memory function include clinical history, seizure onset laterality, MRI evidence suggesting hippocampal sclerosis, Wada memory performance, and level of neuropsychological memory performance.

In the present case, there was strong evidence to suggest conflicting memory outcomes. On the one hand, the patient had a history of febrile seizures, consistent unilateral temporal lobe seizure onset, and MRI evidence suggesting hippocampal atrophy, which was subsequently confirmed by pathology. All of these indicated no unusual risk to memory function following temporal lobectomy given the evidence of structural disease that was to be included in the resection. In contrast, high verbal memory and bilaterally normal Wada memory performance suggested increased risk for postoperative memory decline, particularly for a patient undergoing resection of the left medial temporal lobe.

Examination of separate indices indicated a decline in Delayed Auditory Memory to 108, with an increase in Delayed Visual Memory to 122 1 year after surgery. Examining only the general summary memory from the WMS-III would lead to incorrect conclusions because the postoperative decline in verbal memory was offset by significant practice effects associated with the Visual Memory indices. Although E.G.'s Delayed Visual Memory index increased from 100 at baseline to 115 at the 2-month followup and to 122 1 year following surgery, the 22-point improvement still falls within the 90% confidence interval of reliable change based on a 7.5-month follow-up interval [19]. On the Selective Reminding Test, Continuous Long-Term Retrieval decreased to 23/72, and 30-minute delayed free recall decreased to 7/12 at 2 months following surgery. In contrast, Complex Figure Recall, using an alternative figure, was unchanged at 29/36.

The discrepant postoperative memory risk indicators were discussed repeatedly at length with the patient and his parents, who were told that one option would be to return to school and acquire the necessary vocational skills needed for computer science prior to eventual surgery due to the risk to postoperative memory decline. Also discussed was the effect of a possible decline in

memory to more average scores on daily function. They were counseled with speculative results that the magnitude of memory change, in addition to the specific level of postoperative performance, would be a critical factor with respect to the effects of memory decline on daily function. Interestingly, this is exactly the pattern of memory change subsequently experienced by E.G.

Following surgery, E.G. returned to school but found that his coursework was much more difficult. He subsequently changed his major from computer science and, by his 1-year follow-up examination, had not declared a new major. Although he had experienced a single seizure approximately 3 weeks after surgery, he was subsequently seizure-free and was driving at the time of his 1-year follow-up assessment. E.G. was adamant that if he had it do over again, knowing the cognitive outcome, he would make the same decision. This is reflected in the significant increase in his Quality of Life score from  $T = 47$  (41st percentile) to  $T = 61$  (86.5th percentile). It would be interesting if this high level of satisfaction with surgery persists throughout his life span given the accelerated memory decline with normal aging in patients who had undergone temporal lobectomy decades previously [20].

Although patients at risk for postoperative amnesia can generally be identified by history, imaging, and clinical findings, there is often a need to predict patients at risk for significant memory decline, which, although not sufficiently severe to be considered global amnesia, is nevertheless of sufficient severity to disrupt social or occupational functioning. The traditional concern of whether the temporal lobe contralateral to the proposed resection is sufficiently functional to sustain memory function has been termed by Chelune as “functional reserve” [21]. However, the functional adequacy of the medial temporal lobe included in resection also contributes to postoperative memory change if functional tissue still contributing to recent memory formation is removed.

Significant functional adequacy of the left medial temporal lobe can be inferred with neuropsychological testing from either normal verbal and nonverbal memory or normal verbal memory but poor nonverbal memory, a pattern typically associated with right temporal seizure onset. Our patient had normal verbal memory suggesting significant functional adequacy of the left medial temporal lobe.

On Wada testing, functional adequacy is assessed by memory performance following injection contralateral to the seizure onset [13]. Patients with good Wada memory performance following contralateral injection, or those with smaller ipsilateral–contralateral memory asymmetries, are more likely to display significant postoperative memory decline [12,13]. Thus, in contrast to the idealized Wada memory performance in which performance is high following injection ipsilateral to the seizure focus with impairment of memory during the contralateral study, good memory scores following

the contralateral amobarbital injection suggest that the temporal lobe containing the seizure focus is still actively contributing to memory formation. E.G. also had a Wada pattern suggesting significant functional adequacy of the left medial temporal lobe, with a Wada memory recognition score of 8/8.

#### 4. Summary

This case illustrates the nonredundancy of functional and structural measures of hippocampal status in the evaluation for ATL. In the patient described here, behavioral measures of neuropsychological memory testing and Wada memory testing correctly forecast the risk of memory change despite contradictory information from imaging and seizure variables. Consequently, behavioral measures, at least in the present case, appear more valuable than structural measures in predicting cognitive change following surgery, and suggest that normal behavioral memory measures should alert the clinician to the risk of memory decline following left ATL, even in the presence of hippocampal atrophy and consistent left temporal seizure onset.

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