Epilepsy & Behavior Reports 18 (2022) 100515

Contents lists available at ScienceDirect

Epilepsy & Behavior Reports

journal homepage: www.elsevier.com/locate/ebcr

Case Report

"Is this normal after such a major surgery?" Memory complaint after right temporal lobe excision in an adolescent

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ARTICLE INFO

Article history:
Received 4 October 2021
Revised 17 November 2021
Accepted 2 December 2021
Available online 8 December 2021

Keywords:
Subjective memory complaint
Depression
Temporal lobectomy

ABSTRACT

Memory deficits are commonly associated with temporal-lobe epilepsy. Memory may worsen after surgical resection of the temporal lobe. Risk factors for decline are structural integrity of the mesial temporal lobe structures and intact pre-operative memory. Subjective memory complaints are influenced by depression or other psychological disorders. A 16-year-old girl underwent resection from the right lateral and medial temporal lobe and after surgery she complained of a significant memory impairment, which was unexpected given her baseline assessment. Before undertaking a neuropsychological assessment, she was referred for a psychiatric consultation which revealed depression, leading to treatment with antidepressant medication. Over time she also admitted to severe headaches and inadequate sleep. With these issues addressed, assessment indicated memory performance had not changed relative to her pre-operative baseline with stability or improvement in memory across longitudinal assessments. This case illustrates the contribution of mood state and other potential factors in contributing to subjective memory complaints.

Introduction

The major cognitive complaint of people with temporal lobe epilepsy is memory dysfunction, reflecting the critical role of the lateral and medial temporal lobe structures in memory [1,2]. In the neuropsychological assessment of surgical cases, the nature of the memory impairment is a key indicator in localizing and lateralizing neural dysfunction and providing prognostic indicators of the cognitive risks of epilepsy surgery [3,4]. Performance on verbal learning and verbal memory tasks may reliably distinguish between left and right temporal lobe dysfunction, with impairments more likely in the former; on the other hand, visual-spatial memory impairments may signal right temporal lobe dysfunction, but is overall a less reliable indicator of such specificity [3–5]. In children, the nature of pre-operative memory performance may not distinguish between those with left and right temporal lobe epilepsy, although it appears that memory deficits become more pronounced and lateralized during adolescence [6–10].

A number of variables have been identified that are predictive of memory outcomes after temporal lobectomy [1]. In both children and adults, better memory before surgery is a risk factor for decline after surgery [9,11,12]. The structural integrity of the hippocampus is also important, with decline less likely in those with pre-existing pathology [11–13]. Decrements in verbal memory have been documented in children and adolescents in whom resections included the left mesial temporal lobe structures [6,9]. A systematic review of cognitive outcomes after surgery in adults found that the average rate of verbal memory decline was 44% after left temporal-lobe resections, and 20% after right resections, whereas a decline in visual memory was similar for both left and right temporal resections (23% and 21%, respectively) [14], figures that corresponded closely with the findings from a large cohort (n = 732) of patients from a surgical center in Bonn [5]. In adults, anterior temporal lobectomy is associated with greater memory loss than tailored resections (lesionectomy or selective amygdalohippocampectomy [5]. A systematic review of studies of children who had temporal-lobe excisions indicated that the majority remained stable with respect to memory function after surgery, but the review did not present data on differential rates of decline related to laterality of resection or type of memory stimuli [15].

It must also be recognized that patient's subjective complaints of memory difficulty may reflect symptoms of depression or anxiety in addition to, or even instead of, neurocognitive mechanisms [16]. In people with epilepsy, subjective cognitive complaints have

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https://doi.org/10.1016/j.ebr.2021.100515
2589-9864/

been linked to psychological disorders, number of antiseizure medications, and seizure frequency, but not necessarily to performance on objective cognitive measures [17,18].

The case presented here illustrates the importance of considering a range of factors in evaluating the memory outcomes of epilepsy surgery. The contribution of a number of the variables discussed above in determining the short and long-term outcomes of temporal lobe resection in an adolescent is highlighted.

Case report

This study was approved by the Research Ethics Board of the Hospital for Sick Children.

A 16-year-old right-handed girl was referred for a neuropsychological assessment as part of her diagnostic evaluations to determine whether she was a candidate for epilepsy surgery. At the time she was completing her second-to-the-last year of high school and was an average student.

Early developmental history

She was the youngest of three children. Her parents were university-educated and employed in professional jobs. Early medical and developmental history revealed that she was born at term after a normal pregnancy and delivery. Apart from some clumsiness as a toddler, her parents reported that her development was unremarkable and that she met her milestones as expected. She did, however, have some behavioral problems and she was diagnosed with attention deficit hyperactivity disorder and treated with methylphenidate, which she took until the age of 13 years. She had undergone a psychoeducational assessment at the age of 7 years due to her difficult behavior; the assessment revealed superior nonverbal abilities and average verbal abilities and academic skills within normal limits. As part of the assessment around the diagnosis of ADHD, she had an EEG which demonstrated a right temporal lobe abnormality but was not interpreted as epileptiform in nature. At the age of 8 years, she experienced dejá vu episodes several times a day, which were attributed to her ADHD. Parents could not recall how long these episodes persisted.

Seizure history and medical investigations

At the age of 14 years, 9 months she had a focal to bilateral tonic-clonic seizure with loss of consciousness; she was started on antiseizure medication, first with phenytoin and a month later leviteracetam was added. She continued to have seizures (although no more of the focal to bilateral tonic-clonic ones) from one to three times per day. There were two types of seizure semiologies reported. In the first, she described feeling disembodied, although she reported she could not see her own body. During these events moving her body made her "feel weird" although she reported being able to continue to control her body. At times these events evolved whereby she felt pressure on her chest and subjectively found it difficult to control her body so that she would stand still and wait for the seizure to stop. She described that the second began like the first but evolved to include left facial jerking movements with head deviation to the left followed by left face and arm clonic movements; post-ictally she was lethargic. Because of the persistence of seizures, she was referred for investigations to determine if she was a candidate for epilepsy surgery.

Neuroimaging revealed a lesion in the right medial temporal lobe, thought to be a tumor (neuropathology after surgery confirmed a low-grade astrocytoma). EEG demonstrated a right temporal lobe focus, and MEG recorded 27 dipoles, 26 of them in the right hemisphere (25 of which were in the right temporal lobe). She had an fMRI for language which revealed left hemisphere dominance.

Pre-operative neuropsychological evaluation

During the neuropsychological interview, her parents reported that she had been expressing an increase in anger and opposition at home in the prior several months. Their responses on a behavioral questionnaire (the Child Behavior Checklist) indicated elevations on a scale of oppositional defiant problems (arguing, disobedience, temper). Although these behaviors had been long standing, the parents interpreted the recent increase as a reaction to the diagnosis of epilepsy and the underlying tumor. The only sources of stress reported by the parents were recent diagnosis of epilepsy and the tumor, and the challenging oppositional behavior of their daughter.

The girl herself was cooperative during the assessment on which she worked diligently. In the interview she denied any mood or behavioral issues.

A comprehensive evaluation was undertaken, with tests of intelligence, receptive and expressive language, visual and verbal memory, executive function, academic and fine motor skills administered.

Her IQ was in the average range, and her performance on tests of expressive and receptive language, executive functions, academic skills and hand motor performance were within normal limits. Given the history of abnormality in the right temporal lobe, several tests of memory were administered, assessing verbal learning and recall, and recall and recognition of details of visual stimuli. The memory results are presented in Table 1. Her performance on tests of verbal learning and recall were within normal limits. In contrast she had impairments on tests of visual recall and recognition. Overall, the pattern of results was interpreted as being consistent with the imaging and neurophysiological findings indicative of right temporal lobe abnormality. It was recommended that in at least the first semester upon her return to school, and possibly longer, that she take a reduced course load to allow ample time for recovery. Given her difficult behaviour as reported by her parents, a referral for counselling was made, which she refused.

Surgery and short-term outcome

Given the concordant results across the pre-surgical investigations, she underwent a resection from the anterior right temporal lobe including the amygdala and hippocampus. She did not have seizures after surgery. In follow-up visits to the neurology clinic during the following several months, her parents reported that she was very argumentative and as a result there was a great deal of stress at home. Two months after the surgery she returned to school. Approximately one month later she sent an email to her neurosurgeon complaining of memory problems. She wrote:

> "I find that I am having trouble with my short-term memory. It has been more difficult for me to recall conversations that I had with other people a few hours after speaking to them. This problem gets worse week by week. When I try to recall conversations or events, I feel that I am trying to solve a huge puzzle. When I try to retrace conversations or events, the more time I spend doing so, the pieces to this puzzle start to disappear. Over the past few weeks, I find that these pieces disappear more quickly. I find that if the event affects me personally, like an argument, I will be able to recall the event with no problems, 1 to 1.5 hours later in detail. When trying to recall situations that don't affect me personally like talking to another person, or asking a teacher for help, I find that my memory can vary from 5 minutes to 1 hour. One situation was last week, I asked

Table 1
Verbal and visual memory scores at all assessments. All scores are presented as standard or scaled scores for ease of comparison across tests.

	Timing Relative to Surgery			
	Before	6-mos after	12-mos after	5 years after
Age (years-months)	16–0	16–09	17–03	21–09
Word List Learning[1]				
Immediate Recall	100	117	100	100
Delayed Recall	100	112	100	100
Word Pair Delayed Recall[2]	12	7	12	12
Immediate Recall of Story[2]	13	9	10	16
Delayed Recall of Story[2]	13	9	10	15
Immediate Recognition of Faces[2]	4	4	6	6
Delayed Recognition of Faces[2]	4	9	8	8
Family Pictures Immediate Recall[2]	5	n/a	9	n/a
Family Pictures Delayed Recall[2]	5	n/a	8	n/a

n/a: not administered.
[1] Standard scores: mean of 100, SD of 15 in the general population. Pre-operative and 12-month assessments: California Verbal Leaning Test; 6 month post-operative: Children's Auditory Verbal Learning Test-2; 5 year follow-up: Rey Auditory Verbal Learning Test.
[2] Scaled scores: mean of 10, SD of 3 in the general population. Pre-operative, 12 month and 5-year assessments: Wechsler Memory Scale-3; 6-month post-operative: Children's Memory Scale.

my math teacher a question during my lunch about the lesson taught earlier that morning. I understood the lesson after she explained it to me, then after school I went back to my teacher asking the same question. The only thing I remember was that I asked for help during my lunch, I completely forgot what I asked, and what she told me.

Is this normal after such a major surgery?"

The neurosurgeon made a referral to neuropsychology for follow-up of the memory complaint.

Although some may have recommended a neuropsychological assessment at this point, a different course of action was undertaken. The nature of the memory complaint was not consistent with expectations of outcome after surgery. First, most of the complaint appeared to describe material that was verbal in nature (conversations, content of school lessons). This aspect was unexpected given the nature of the pre-operative pattern of memory results, the confirmation that language was represented in the left hemisphere and the concordance between the neuropsychological results and the imaging, EEG and MEG results. Second, the description of the memory impairment worsening over time did not make sense in light of the resection. At times patients may have a post-operative memory impairment that improves over the several months after surgery due to the reduction of swelling in the brain adjacent to the resection, but reports of worsening are not common. A third consideration in not undertaking a neuropsychological assessment was the parent report of a worsening in her behaviour (increased argumentativeness). For these reasons other factors were considered and the possibility of a psychiatric contribution to the reported symptoms was raised; it was decided that the first step in dealing with the patient's complaints should be a referral for psychiatric consultation.

Initially she refused the consultation, denying any problems, but relented with parental pressure. The psychiatrist described behavioural changes in context of long standing apparent emotional and behavioural issues. Additionally, a diagnosis of depression was made and sertraline was prescribed.

Three months later (a total of six months after surgery), she was seen for an abbreviated neuropsychological assessment to examine memory and to screen for any unexpected language declines (given that the memory complaints had largely been verbal in nature). She admitted that she had been quite depressed even in the period when she had refused the psychiatric consultation. Furthermore, she now also revealed that after surgery she had experienced severe headaches daily, and that these prevented her from concentrating. Her sleep habits were poor, with a late bedtime, resulting in her feeling very tired in the morning when she had to go to school. She had not taken the advice to reduce her course load and she had failed two subjects in her first semester. However, she reported that both her depression and her headaches had improved somewhat, as had her memory. There had been no change in her anti-seizure medications since her surgery.

The neuropsychological assessment revealed that her language skills were unchanged relative to her pre-operative performance. Alternate forms of a subset of the memory tests from the first assessment were administered. The results, shown in Table 1, revealed that her verbal learning and recall scores were varied; her list learning and recall were higher than the previous scores, but her word pair recall and story recall scores were lower (although both within normal limits). Her immediate recognition of faces remained impaired but her delayed recognition now fell within the average range. Overall, her performance was not sufficient to explain the significant memory impairment in daily life that she had reported several months earlier, supporting the hypothesis that her subjective memory complaints were likely secondary to her depression. The new information that she revealed about her headaches and inadequate sleep added information about other likely contributors. Recommendations were made for school accommodations, treatment of the headaches, and establishing improved sleep habits.

One-year post surgical follow-up

A full neuropsychological assessment was completed one year after surgery. She continued to take sertraline, and reported continued improvement with respect to her mood, memory and headaches, although the headaches did become worse in times of stress, such as studying for exams. She had been seizure-free since surgery and had discontinued leviteracetam but remained on phenytoin.

This assessment did not reveal any detrimental effects of surgery on her cognition. Her IQ, language, academic and executive function scores remained in the average range, and did not differ from her pre-operative levels. Scores on the memory tests are presented in Table 1. Her recall of a word list was average; although her score was lower than it had been at the 6-month follow-up, it was average and was identical to her pre-operative score (the discrepancy may have been due to the use of a different version of the word learning test at the shorter-term follow-up assessment). Recall of the details of stories was average. Recognition and recall of visual information were somewhat improved relative

to her pre-operative baseline. Parents continued to report oppositional defiant behaviours.

Long-term follow-up

Five years after her surgery she consented to participate in a study on long-term surgical outcomes, which included a brief cognitive assessment. She was in university, taking no antiseizure medication and experienced on average one brief aura per year. She reported high satisfaction with having had surgery. IQ, academic and language skills remained within normal limits, comparable to the results documented in earlier assessments. Verbal recall was within the average to above average range, and her recognition of faces was identical to the score obtained in the one-year follow-up (see Table 1). Her parents again rated her within the clinical range for aggressive and oppositional behaviours (using the adult version of the Child Behavior Checklist). Self-report on a depression screening inventory was within normal limits.

Discussion

This case was an adolescent girl who underwent epilepsy surgery and in the post-operative phase complained of a significant memory impairment. Investigation uncovered a diagnosis of depression, and the presence of severe headaches and poor sleep. Serial neuropsychological evaluation revealed no decline in memory on objective measures, suggesting her subjective memory complaints were not an effect of surgery per se.

This case illustrates the need to take a comprehensive view of the multitude of factors that can influence everyday memory in addition to the seizures, underlying neural substrate and antiseizure medications that are known risk factors for memory impairment. Research has demonstrated that people with epilepsy may report subjective memory problems and that these symptoms are not necessarily correlated with objective memory performance. These complaints have been found to be more strongly related to mood and anxiety disorders or other sources of psychological distress [3,18–20]. Symptom validity testing, the use of measures to evaluate the validity and response biases in relation to symptom reporting [21,22] was not used in the assessment of this girl, but may have been useful, particularly if an assessment had been conducted in the early post-operative phase when she was complaining of memory impairment.

Depression has been linked with self-reports of memory problems in people with epilepsy [3,18–20]. Depression is the most common psychiatric comorbidity in epilepsy, with almost one third of patients experiencing a depressive episode in their lifetime; after surgery, depressive episodes are more likely to occur in individuals with a pre-existing history of mood disorders [23]. Although depression may improve after surgery, approximately 10–30% of patients who have undergone temporal lobe resections have reported de novo depression in the first 3 months post-operatively [24–26]. This teenager denied any symptoms of mood disorder prior to surgery, and her parents had not endorsed significant symptoms of depression on the questionnaire they completed. However, after surgery she had also initially denied feeling depressed although eventually admitted to significant depressive symptomatology. Thus, it is unclear whether the depression was of new onset or a continuation of previously denied symptoms.

In addition to depression, this girl eventually reported experiencing severe daily headaches after her surgery. It is conceivable that these headaches could have also contributed to her memory difficulties, and the pain may have interfered with her ability to pay attention and with the mental effort required by recall. Chronic headaches are associated with encoding and recall impairments and furthermore, can contribute to mood disorders [27,28]. One study in people with new onset epilepsy found that that migraine comorbidity and objective memory performance were not associated; there was, however, an association between migraine comorbidity and subjective memory complaints, a relationship that was mediated by depression and anxiety symptoms [29].

Another factor conceivably related to the postoperative memory complaints was poor sleep hygiene. She did not spontaneously offer information about her sleep, but upon probing she reported that her sleep pattern was marked by going to bed very late at night so that she was exhausted in the mornings at school. Long-term memory consolidation is a major function of sleep [30]. The importance of sleep for memory in patients with epilepsy has also been demonstrated [31–33]. The fatigue resulting from insufficient sleep may have also interfered with her attention and ability to sustain mental effort, resulting in poor encoding.

Prior to surgery and at the 6-month follow-up assessment this girl was on two anti-seizure medications, phenytoin and leviteracetam. Although the former has been associated with cognitive side effects, these effects are seen largely on measures of motor speed and reaction time and not of memory [34,35]. She did not have impairments on tests reliant on psychomotor speed at any of her assessments. The side effects most commonly reported for leviteracetam are irritability and moodiness, although it has also been associated with depression [34,36]. Leviteracetam may have contributed to the behavioral challenges reported by her parents, although her difficult behaviour did pre-date the diagnosis of her epilepsy and start of medication. There was, however, no change in her medications (relative to her pre-operative regimen) at the time that she was maximally complaining of memory deficits, nor at the six-month follow-up, making it difficult to attribute her recent complaints to these medications.

One limitation of this case report was the need to use different test forms at the 6-month follow-up due to concerns about familiarity and practice effects. In addition, a different list-learning test was used at the 5-year follow-up. All test forms were comparable in demands (e.g. list learning with repetition and recall, story recall, recognition of photographs of faces) and yield results that are highly correlated. Across assessments the results were consistent in demonstrating normal verbal memory function, which was in contrast with her subjective complaints after surgery. Another limitation was the lack of information on family history of depression or other mental health disorders.

Conclusions

This case illustrates the importance of considering multiple factors in the evaluation of memory complaints after temporal lobe surgery. Although surgery may represent a risk for memory decline in some patients, with both verbal and visual memory loss possible after resections of either the left or right temporal lobe structures, not all memory complaints are related to surgery. In this case, depression, headaches and inadequate sleep were likely contributors. Neuropsychologists should be aware of these factors which can determine the timing of recommended assessments and appropriate referrals for diagnosis and care.

Ethical Statement

This manuscript presents data collected as a part of routine clinical care, and was approved by the Research Ethics Board of the Hospital for Sick Children in accordance with their guidelines for publication of retrospective clinical data.

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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