doi: 10.2176/jns-nmc.2021-0175
Neurol Med Chir (Tokyo) 62, 286-293, 2022
Online April 12, 2022

Effect of Early Surgical Intervention for Brain Tumors Associated with Epilepsy on the Improvement in Memory Performance

Tsukasa Hirano,[1] Hime Suzuki,[1] Katsuya Komatsu,[1]
Aya Kanno,[1] Yuusuke Kimura,[1] Rei Enatsu,[1]
Satoko Ochi,[1] Hirofumi Ohnishi,[2] and Nobuhiro Mikuni[1]

[1]*Department of Neurosurgery, Sapporo Medical University, Sapporo, Hokkaido, Japan*
[2]*Department of Public Health, Sapporo Medical University, Sapporo, Hokkaido, Japan*

Abstract

We evaluated the effect of early surgical intervention on the change in memory performance of patients with low-grade brain tumors associated with epilepsy. Twenty-three adult patients with low-grade brain tumors and epilepsy who underwent surgery at our institution between 2010 and 2019 were included. The Wechsler Memory Scale-Revised (WMS-R) was used to assess cognitive memory performance. Memory performance before and after surgery was retrospectively evaluated. In addition, the relationships among preoperative memory function, postoperative seizure outcome, preoperative seizure control, temporal lobe lesion, and change in memory function were examined. There were statistically significant improvements from median preoperative to postoperative WMS-R subscale scores for verbal memory, general memory, and delayed recall ($p<0.001$, $p<0.001$, and $p=0.0055$, respectively) regardless of preoperative sores and tumor location. Good postsurgical seizure control was associated with significant improvements in postoperative WMS-R performance. Our results indicated that early surgical intervention might improve postoperative memory function in patients with low-grade brain tumors and epilepsy.

Keywords: epilepsy, epilepsy with brain tumor, memory performance

Introduction

The cognitive benefits of good epileptic seizure control have been studied in intractable epilepsy. Patients with chronic epilepsy often develop cognitive impairment.[1-3] The occurrence of seizures in childhood is associated with increased risk of social and educational problems and death.[4] However, there are few comprehensive reports on epilepsy associated with brain tumors, and early surgical intervention remains controversial.[5,6] In patients who undergo surgical treatment for epilepsy, postoperative cognitive performance is frequently evaluated using validated cognitive and memory tests. Some studies have reported improvement, whereas others have reported deterioration.[7-14] Therefore, there is uncertainty about whether surgical treatment for epilepsy improves cognitive function. Pharmacotherapy is the first option for treating most patients with epilepsy, but some patients do not respond to antiseizure medications (ASMs). Clinicians should consider early surgical intervention if gross total resection can be achieved because it can lead to effective seizure control and eventual discontinuation of ASMs.[15-17] If seizures remain uncontrolled for more than 2 years after the initial seizure despite the use of ASMs, patients are considered to have intractable epilepsy.[18] After this period of pharmacotherapy, patients are often referred to epilepsy surgeons. As mentioned above, early surgical intervention is desirable due to the possibility of good seizure control, especially for epileptic seizures associated with low-grade brain tumors. However, neurosurgeons, especially epilepsy surgeons, are not always available for the initial intervention in patients with epileptic seizures. The time to surgery depends largely on the time to consultation. Therefore, it is important to educate neurologists to consult neurosurgeons as

Received June 10, 2021; Accepted February 15, 2022

early as possible for patients with epilepsy who have low-grade brain tumors. It is also important for neurosurgeons to have the option of performing early surgical intervention after consultation. At our institution, the treatment strategy for non-malignant brain tumors associated with epilepsy is to perform early surgical intervention in anticipation of possible intractable epilepsy and to achieve effective seizure control. In this study, we examined how early surgical intervention for low-grade brain tumors with epilepsy affects cognitive function, especially postoperative memory function.

Materials and Methods

Patients

The inclusion criteria were as follows: (i) craniotomy for a brain tumor with seizure onset diagnosed at the Sapporo Medical University Hospital between 2010 and 2019, (ii) age at surgery of 20 years or above, and (iii) availability of preoperative total and composite subscale WMS-R[19] scores. Brain tumors were defined as low-grade tumors such as ganglioglioma, diffuse astrocytoma, oligodendroglioma, and cerebral cavernous malformation.[20] Patients were eligible for study inclusion if they could be followed for at least 1 year. Patients were excluded from the study if (i) either preoperative or postoperative data were missing, (ii) the WMS-R was administered only in the early postoperative period and the results did not rule out a learning effect, or (iii) valid WMS-R testing was not possible due to the patient's age or severe mental deterioration.

Seizure outcome was assessed based on seizure frequency at 1 year after surgery. Postoperative seizure outcomes were categorized by seizure frequency as follows. Patients who experienced 0-1 seizures during the year after surgery were classified into the good seizure outcome group. Patients with 2 or more seizures during the year after surgery were classified into the poor seizure outcome group. Regarding reductions in ASM use after surgery, our department's policy was essentially to wait for 2 years after surgery before tapering medications based on the patient's background.

Patient background and demographic factors that were analyzed in this study included age; sex; laterality of surgery; lobe of seizure origin; pathological diagnosis; invasion of the hippocampus, mammillary body, and corpus callosum; preoperative seizure control; number of ASMs at the time of surgery; number of days from the first epileptic seizure to surgery; number of days from the first outpatient consultation at our hospital to surgery; and number of days from surgery to WMS-R examination. Preoperative seizure control was categorized by seizure frequency as follows: patients who experienced 0 or 1 epileptic seizure after their first seizure were classified as having good seizure control and those with 2 or more seizures after their first seizure and before surgery were classified as having poor seizure control. This retrospective study was approved by the ethics committee of the Sapporo Medical University Hospital (approval number 322-201).

Comparison of preoperative and postoperative WMS-R scores

The preoperative and postoperative WMS-R subscale scores of each patient were compared to determine whether there was a significant improvement with surgery. Using a cutoff score of 85, the lower limit of normal (LLN), the impact of the preoperative WMS-R scores on the postoperative WMS-R scores was compared between patients with and without good postoperative seizure control. Moreover, preoperative and postoperative WMS-R scores were compared between patients with and without good postoperative seizure control. To investigate the relationship between preoperative seizure control and postoperative changes in memory function, the ratios of preoperative to postoperative WMS-R subscale scores were used to examine differences in score improvement based on preoperative and postoperative seizure control, respectively. The WMS-R was administered by an occupational therapist within 2 months to 1 year after surgery.

Patients with temporal lobe lesions

Among the eligible patients, WMS-R subscale scores were compared before and after surgery only in patients with temporal lobe lesions. Patients with improvements of 10% or above in preoperative versus postoperative WMS-R subscale scores were classified into the functional improvement group. Patients with improvements of less than 10% were classified into the non-functional improvement group. The relationship between functional improvement status and each background factor was examined. To examine differences between the left and right hemispheres, the preoperative to postoperative ratios of the WMS-R scores were statistically compared by hemisphere.

Statistical analysis

To test for possible selection bias between patients with and without good postoperative seizure control, the distribution of sex, laterality of surgery, and pre-seizure control were analyzed using Fisher's exact test. Similarly, the distribution of lobe of seizure origin, pathological diagnosis, number of ASMs at the time of surgery, and invasion of hippocampus, mammillary body, and corpus callosum were analyzed using the chi-squared test. The distribution of age, number of days from the first epileptic seizure to surgery, number of days from the first outpatient consultation at our hospital to surgery, and number of days from surgery to WMS-R examination were analyzed using the Mann-Whitney *U* test. Preoperative to postoperative changes in median WMS-R subscale scores were compared using the Wilcoxon signed-rank test. P-values < 0.05 were considered statistically significant. All statistical analyses

Table 1 Patient profile

		All (n=23)	Good seizure outcome (n=19)	Poor seizure outcome (n=4)	p-value
Age, years		33.0 (24.0-36.0)	34.0 (29.0-36.0)	37.5 (20.2-54.7)	0.5968
Sex	Male	12	10	2	1
	Female	11	9	2	
Laterality of surgery	Right	12	10	2	1
	Left	11	9	2	
Location	Frontal	6	4	2	0.4481
	Temporal	13	12	1	
	Parietal	3	2	1	
	Occipital	1	1	0	
Pathology	CCM	6	6	0	0.0075
	GG	7	7	0	
	DA	4	1	3	
	OG	6	5	1	
Number of ASMs	1	20	17	3	0.6787
	2	3	2	1	
	≥3	1	1	0	
Pre-seizure control	Good	15	12	3	1
	Poor	8	7	1	
Days		111 (40-351)	188 (47-516)	35 (29.2-91)	0.0566
Pre-op days		35 (29-76)	42 (29-104)	32 (15.7-64.7)	0.3502
Examination days		93 (65-224)	93 (65-224)	122 (63-214)	0.7764

Each value describes the median and interquartile range. CCM: cerebral cavernous malformation, GG: ganglioglioma, DA: diffuse astrocytoma, OG: oligodendroglioma, ASM: antiseizure medication, Days: number of days from the first epileptic seizure to surgery, Pre-seizure control: preoperative seizure control, Pre-op days: number of days from the first outpatient consultation at our hospital to surgery, Examination days: number of days from surgery to Wechsler Memory Scale-Revised testing.

were performed using JMP Pro 15 software (SAS Institute, Cary, NC, USA).

Results

Patients

There were 30 patients diagnosed with low-grade brain tumors and seizure onset who underwent surgery between 2010 and 2019, of whom 23 (12 males and 11 females) were included in the analysis. Table 1 summarizes the background and demographic factors of the study patients by seizure outcome. Patients with and without good postoperative seizure control were evenly distributed in terms of age, sex, laterality of surgery, lobe of seizure origin, preseizure control, and number of ASMs. Pathological diagnosis was significantly associated with postoperative seizure outcome (p=0.0075). Diffuse astrocytoma was strongly associated with poor postoperative seizure control. The median number of days from the first epileptic seizure to surgery, median number of days from first outpatient consultation at our institution to surgery, and median number of days from surgery to WMS-R examination were not significantly different between the two seizure outcome groups (p=0.0566, p=0.3502, and p=0.7764, respectively). Most patients were treated within a short time from the onset of the disease (median, 111 [interquartile range, 40-351]). The age at surgery was almost equal to that at first seizure. Of the 23 patients, 2 had tumor invasion of the corpus callosum, 4 had invasion of the hippocampus, and none had invasion of the mammillary bodies. Regarding the extent of tumor removal, most gangliogliomas and cerebral cavernous malformations and surrounding hemosiderin deposits were almost completely removed. For diffuse astrocytoma and oligodendroglioma, patients with partial resection were included because in some cases the tumor extended into a functional area.

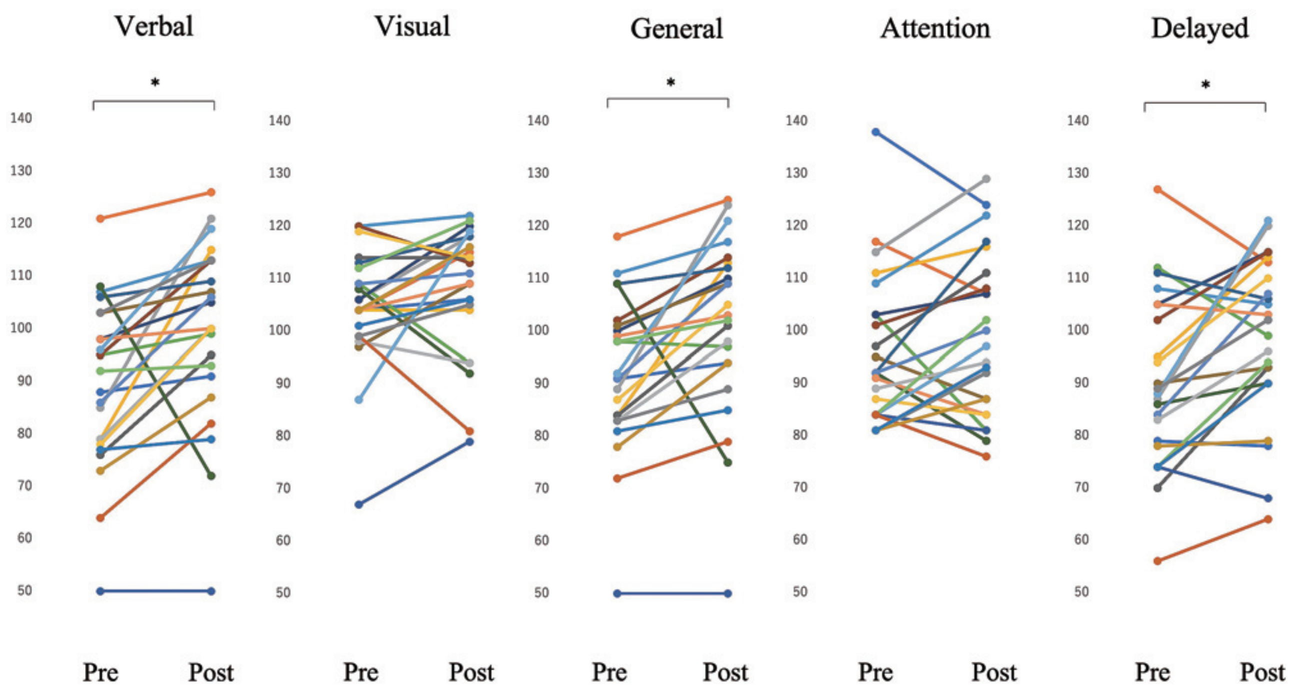

Fig. 1 Preoperative and postoperative WMS-R subscale scores. Patients had improved WMS-R subscale scores for verbal memory, general memory, and delayed recall; p<0.05 was considered statistically significant.

Table 2 Differences in WMS-R subscale score improvement by preoperative WMS-R scores

	Preoperative WMS-R score	Preoperative score	Postoperative score	p-value
Verbal memory	<85	76.5 (66.2-78.7)	87 (78.5-100)	0.0156
	≥85	98 (92-106)	107 (99-113)	0.0073
Visual memory	<85	-	-	-
	≥85	105 (100.5-112.2)	112 (104.7-118)	0.2181
General memory	<85	82 (73.5-83.7)	91.5 (80.5-100.2)	0.0156
	≥85	99 (91-109)	109 (102-117)	0.0081
Attention	<85	84 (81-84)	92 (81-97)	0.1094
	≥85	99 (92-110.5)	107 (84.7-116.7)	0.7541
Delayed recall	<85	74 (72-81)	90 (73-95)	0.0313
	≥85	98.5 (88.7-108.7)	108 (101.2-115)	0.1073

Each value describes the median and interquartile range. WMS-R: Wechsler Memory Scale-Revised

Comparison of preoperative and postoperative WMS-R scores

The preoperative to postoperative WMS-R subscale score changes are graphically presented in Fig. 1. In the 23 patients, there were statistically significant improvements from median preoperative to postoperative WMS-R subscale scores for verbal memory (92-100), general memory (91-103), and delayed recall (88-102) (p<0.001, p<0.001, and p=0.0055, respectively). No significant changes were found in median scores for visual memory (104-111) or attention/concentration (92-97) (p=0.1563 and p=0.2498, respectively).

Table 2 summarizes the preoperative and postoperative WMS-R subscale scores by preoperative WMS-R score (normal, ≥85 versus impaired, <85). Patients who scored less than 85 on each preoperative WMS-R subscale had statistically significant improvements in postoperative scores for verbal memory, general memory, and delayed recall (p= 0.0156, p=0.0156, and p=0.0313, respectively). No significant changes were observed in attention/concentration (p= 0.1094). For visual memory, there was only one corresponding patient who scored less than 85; thus, statistical analysis was not performed. Patients who scored 85 or higher on each preoperative WMS-R subscale had statisti-

Table 3 Preoperative and postoperative WMS-R subscale scores by postoperative seizure outcome status

	Good seizure outcome (n=19)			Poor seizure outcome (n=4)		
	Preoperative score	Postoperative score	p-value	Preoperative score	Postoperative score	p-value
Verbal memory	92 (79-98)	105 (95-113)	<0.0001	83.5 (53.5-106.7)	77 (55.5-105.2)	1
Visual memory	106 (104-113)	114 (106-118)	0.0508	99 (75-105.7)	86.5 (79.5-101.7)	0.625
General memory	92 (84-101)	109 (98-114)	<0.0001	77.5 (55.5-102.5)	77 (56.2-86.5)	1
Attention/concentration	95 (87-109)	102 (87-116)	0.1530	84 (81.7-90)	80 (76.5-89.2)	0.001
Delayed recall	90 (79-105)	105 (93-114)	0.0137	80 (60.5-88.2)	79 (65-99)	0.375

Each value describes the median and interquartile range. WMS-R: Wechsler Memory Scale-Revised

cally significant improvements in postoperative scores for verbal memory and general memory (p=0.0073 and p=0.0081, respectively). No significant changes were observed in visual memory, attention/concentration, or delayed recall (p=0.2181, p=0.7541, and p=0.1073, respectively). Table 3 summarizes the preoperative and postoperative WMS-R subscale scores of patients with versus without good postoperative seizure control. There were significant postoperative improvements in scores for verbal memory, general memory, and delayed recall in patients with good postoperative seizure control (p<0.0001, p<0.0001, and p=0.0137, respectively). However, in patients with poor postoperative seizure control there were no significant postoperative improvements in the scores for any subscale. There were no statistically significant differences in WMS-R subscale score improvements between patients with good and poor preoperative epileptic seizure control (Supplementary Table 1).

Patients with temporal lobe lesions

Thirteen patients with temporal lobe lesions were included in this study. Table 4 presents a summary of these 13 patients. Of the 8 patients with poor preoperative seizure control, 7 had temporal lobe lesions. On the other hand, good postoperative seizure outcomes were achieved in 12 of 13 patients with temporal lobe lesions. With regard to changes in preoperative to postoperative WMS-R subscale scores, there were statistically significant improvements in scores for verbal memory (95-105), general memory (91-105), and delayed recall (89-105) (p=0.0002, p=0.0005, and p=0.0349, respectively). Scores for visual memory (106-114) and attention/concentration (97-107) showed no significant improvement (p=0.1919 and p=0.1223, respectively). Based on a cutoff of 10% to indicate improvement, there were no differences in most background factors between patients with versus without postoperative improvement in WMS-R scores for verbal memory, general memory, or delayed recall (Supplementary Table 2). Patients who had 10% improvement or above in delayed recall scores tended to be older (p=0.0095). There were statistically significant differences observed in preoperative to postoperative ratios of WMS-R scores by hemisphere (Supplementary Table 3).

Discussion

In this retrospective study, we found that early surgical intervention improves postoperative WMS-R subscale scores in patients with low-grade brain tumors associated with epilepsy. Even in patients whose preoperative memory function was at the LLN, improvement to the upper limit of normal was observed. Improvements in WMS-R scores might be more pronounced in patients with good postoperative seizure control. On the other hand, the degree of improvement in postoperative WMS-R subscale scores was not dependent on preoperative control of epileptic seizures. In the analysis limited to patients with temporal lobe lesions, improvement in memory function was expected; this was also true for patients with hippocampal infiltration and medial temporal lobe resection. Although the timing of surgery for brain tumors associated with epilepsy has been controversial, the results of this study might provide evidence of the benefits of early surgical intervention.

In this study, postoperative WMS-R performance was better than preoperative WMS-R performance, even when the preoperative WMS-R scores were below the LLN (i.e., <85). Specifically, significant improvements were observed in scores for verbal memory, general memory, and delayed recall. Our results are not in agreement with those of several previous studies showing that cognitive deficits after surgery generally remained stable over time despite effective postoperative seizure control.[21-23] This discrepancy might be explained by the hypothesis that memory plasticity is preserved to a greater extent than plasticity in other cognitive domains such as executive function in patients with chronic epilepsy. Although it has been reported that ASMs might have neuropsychological effects,[24,25] the number of ASMs did not affect the results in this study, which might have been due to the short time between the onset of epilepsy and surgery (median, 111 [interquartile range, 40-351] days) and the fact that most ASMs used were new antiepileptic drugs such as levetiracetam, which are less likely to affect cognitive function. In this study, the WMS-R

Table 4 Profile and differences in preoperative and postoperative WMS-R scores in patients with temporal lobe epilepsy

Age, years	Sex	Pathology	Days	Pre-op days	Laterality of surgery	Invasion of hippocampus	MTLR	Number of ASMs	ASMs	Pre-seizure control	Seizure outcome	Verbal memory preoperative score	Verbal memory postoperative score	Visual memory preoperative score	Visual memory postoperative score	General memory preoperative score	General memory postoperative score	Attention/concentration preoperative score	Attention/concentration postoperative score	Delayed recall preoperative score	Delayed recall postoperative score
16	M	DA	29	11	R	-	-	2	LEV VPA	×	×	103	113	99	105	83	89	81	92	89	102
24	F	CCM	586	584	L	-	-	1	LTG	×	◯	76	95	114	114	84	101	97	111	70	93
25	M	CCM	2393	45	L	-	-	1	LEV	×	◯	77	79	101	106	81	85	81	93	74	90
34	M	DA	111	15	L	+	+	1	LEV	×	◯	73	87	104	116	78	94	81	87	78	79
36	M	GG	52	35	L	+	-	1	CBZ	◯	◯	88	91	104	106	91	94	138	124	79	78
17	M	GG	238	29	L	-	-	1	LEV	◯	◯	85	121	106	118	89	124	115	129	87	120
24	M	OG	39	34	R	-	-	1	LEV	◯	◯	96	119	87	119	92	121	84	97	88	121
29	F	CCM	188	42	R	-	-	1	LEV	◯	◯	78	100	119	114	87	105	87	84	94	110
35	F	CCM	516	47	R	+	+	1	LEV	◯	◯	95	113	120	113	102	114	101	108	102	115
36	F	GG	114	76	L	-	-	1	LEV	◯	◯	98	105	106	120	100	110	103	107	105	115
36	F	GG	294	64	L	+	+	1	CBZ	×	◯	107	113	120	122	111	117	109	122	108	105
35	M	GG	681	104	L	-	-	2	LEV CBZ	×	◯	106	109	113	118	109	112	92	117	111	106
32	M	CCM	196	30	R	-	-	2	LEV PHT	×	◯	95	99	109	94	98	97	103	81	112	99

WMS-R: Wechsler Memory Scale-Revised, Days: number of days from the first epileptic seizure to surgery, Pre-op days: number of days from the first outpatient consultation at our hospital to surgery, DA: diffuse astrocytoma, CCM: cerebral cavernous malformation, GG: ganglioglioma, OG: oligodendroglioma, MTLR: medial temporal lobe resection, ASM: antiseizure medication, LEV: levetiracetam, VPA: valproic acid, LTG: lamotrigine, CBZ: carbamazepine, PHT: phenytoin, Pre-seizure control: preoperative seizure control.

was administered within the first postoperative year, and ASM use was essentially unchanged during that time. In the longer term, patients can be successfully weaned off ASMs if surgical intervention achieves good seizure control.

When comparing WMS-R scores before and after surgery, the good seizure outcome group had significant improvements in verbal memory, general memory, and delayed recall. By contrast, no significant improvements were observed in the poor seizure outcome group. Although the possibility of selection bias cannot be ruled out due to the small number of patients in the poor seizure outcome group, the study results suggested that seizure outcome might have influenced the WMS-R results. Of the 23 patients, 19 had good seizure control after surgery, suggesting that surgery is a fairly effective treatment strategy for epileptic seizures associated with low-grade brain tumors. Chronic epilepsy causes severe cognitive dysfunction.[3,26,27] Therefore, in order to achieve good seizure control at an earlier stage, surgical intervention to control seizures in patients with intractable epilepsy can partially restore memory function that had been impaired by prolonged, uncontrolled epilepsy.

Similar to the overall results, when the analysis was limited to patients with temporal lobe lesions, significant improvements were observed in verbal memory, general memory, and delayed recall scores after surgery. Because of the small number of patients with temporal lobe lesions in the poor seizure outcome group, we were unable to compare the improvement of memory function before and after surgery by seizure outcome. However, memory function improved in patients with temporal lobe lesions as a whole, supporting early surgical intervention, especially in patients with epilepsy and low-grade brain tumors located in the temporal lobe, which is involved in memory function. Although many patients with temporal lobe lesions had poor preoperative seizure control (7/13; 53.8%), good seizure outcome (12/13; 92.3%) was achieved after surgery. These results suggest that it might be difficult to achieve seizure control in patients with temporal lobe lesions with pharmacotherapy alone, but good seizure control might be easily achieved with surgery. In addition, the study did not identify any patient background factors that affected scores on these items between patients with scores that improved by more than 10% postoperatively and patients with scores that improved by less than 10% postoperatively. The hippocampus is a component of the Papez circuit, a memory pathway, but lesion invasion of this region did not influence outcomes. Similarly, medial temporal lobectomy did not affect outcomes.

Long-term epilepsy-associated tumors (LEATs) are benign neuroepithelial tumors.[20,28] Most LEATs, such as dysembryoplastic neuroepithelial tumors, gangliogliomas, and pilocytic astrocytomas, correspond to World Health Organization (WHO) grade I brain tumors with low proliferative potential. However, their broad neuropathologic spectrum and the absence of distinctive histopathological features make it impossible to classify them based on the WHO brain tumor grading system.[29] LEATs account for 2%-5% of all brain tumors[30] and are the second most common neuropathological finding in epilepsy surgery.[29] Surgical resection of LEATs leads to seizure relief in 60%-100% of patients.[4,31,32] Surgical treatment of LEATs is indicated to control seizures,[1] although their slow-growing nature and benign long-term course suggest that surgical intervention might not be needed to prevent tumor progression.[20,33] Although the duration from first seizure to surgery for LEATs has recently been shortened, it is still reported to be more than 5 years.[29] Early surgical interventions in small children with intractable epilepsy help prevent cognitive deterioration.[27] Surgical treatments are also effective for seizure control in adult patients.[34] Moreover, given the long-term adverse cognitive effects of ASMs, particularly in patients on regimens with multiple drugs,[24] early surgery might be an important option to reduce or completely discontinue the use of ASMs. Our results suggest that surgical treatment of LEATs in adults can help prevent seizures and cognitive deterioration. Furthermore, our results suggest that early surgery contributes to preventing cognitive deterioration and the adverse effects of ASMs.

Several limitations of this study should be noted. First, due to the small number of patients, multivariate analysis could not be performed. In addition, there are many confounding factors such as differences in pathology results and surgical approaches. However, the number of adult patients with epilepsy associated with non-malignant brain tumors who can undergo cognitive function testing is limited. It could be important to discuss the possibility, in terms of improving WMS-R scores, of early surgery for epilepsy being recommended for adults with organic lesions as well as for children. Second, the study used a retrospective design and the postoperative WMS-R test was administered only once, at varying timepoints after surgery. Third, although LEATs are typically defined as tumors that have caused drug-resistant epilepsy for 2 years or longer,[20] patients in our study underwent surgery less than 2 years after disease onset. The standard procedure at our institution is to conduct early surgery for low-grade gliomas in non-elderly patients. Cerebral cavernous malformations in non-functional regions are proactively treated with surgery to reduce the risk of bleeding. Four patients (three cerebral cavernous malformations, one ganglioglioma) had more than 2 years elapsed between their first seizure and surgery, which could not be strictly described as early surgical intervention. On the other hand, patients referred to our outpatient clinic with a diagnosis or suspicion of benign brain tumor with epileptic seizures underwent surgery after a median of 35 days, a relatively short time. Fourth, due to the small size of the poor seizure outcome group, type II error in the poor seizure outcome group cannot be ruled out when comparing by seizure outcome. Fifth, since the WMS-R focuses on the components of memory function,[35,36] our results did not cover a broad spectrum of cognitive functions. Our data suggest that a prospective study with a large cohort of patients with intractable epilepsy is warranted to investigate changes between preoperative and postoperative performance using other cognitive function tests, such as the Wechsler Adult Intelligence Scale, Trail Making Test, Behavioral Assessment of the Dysexecutive Syndrome, and Wisconsin Card Sorting Test.

Conclusion

In patients with brain tumors associated with epilepsy, early surgical intervention might be associated with improved postoperative memory function. This effect can be expected regardless of preoperative functional decline. Good postsurgical seizure control was associated with significant improvements in postoperative WMS-R performance. This retrospective study suggests that early surgical intervention for low-grade brain tumors associated with epilepsy might help maintain or improve cognitive function.

Supplementary Material

https://doi.org/10.2176/jns-nmc.2021-0175

Acknowledgments

None

Conflicts of Interest Disclosure

None

References

1) Thompson PJ, Duncan JS: Cognitive decline in severe intractable epilepsy. *Epilepsia* 46: 1780-1787, 2005
2) Klein M, Engelberts NH, van der, Ploeg HM, et al.: Epilepsy in low-grade gliomas: the impact on cognitive function and quality of life. *Ann Neurol* 54: 514-520, 2003
3) Jokeit H, Ebner A: Long term effects of refractory temporal lobe epilepsy on cognitive abilities: a cross sectional study. *J Neurol Neurosurg Psychiatry* 67: 44-50, 1999
4) Bonney PA, Glenn CA, Ebeling PA, et al.: Seizure freedom rates and prognostic indicators after resection of gangliogliomas: a review. *World Neurosurg* 84: 1988-1996, 2015
5) Pelliccia V, Deleo F, Gozzo F, et al.: Early and late epilepsy surgery in focal epilepsies associated with long-term epilepsy-associated tumors. *J Neurosurg* 127: 1147-1152, 2017
6) Suzuki H, Mikuni N, Sugita S, et al.: Molecular aberrations asso-

ciated with seizure control in diffuse astrocytic and oligodendroglial tumors. *Neurol Med Chir (Tokyo)* 60: 147-155, 2020

7) Chelune GJ: Individual change after epilepsy surgery: practice effects and base-rate information. *Neuropsychology* 7: 41-52, 1993
8) Martin RC, Sawrie SM, Roth DL, et al.: Individual memory change after anterior temporal lobectomy: a base rate analysis using regression-based outcome methodology. *Epilepsia* 39: 1075-1082, 1998
9) Helmstaedter C, Kurthen M, Lux S, Reuber M, Elger CE: Chronic epilepsy and cognition: a longitudinal study in temporal lobe epilepsy. *Ann Neurol* 54: 425-432, 2003
10) Stroup E, Langfitt J, Berg M, McDermott M, Pilcher W, Como P: Predicting verbal memory decline following anterior temporal lobectomy (ATL). *Neurology* 60: 1266-1273, 2003
11) Rausch R, Kraemer S, Pietras CJ, Le M, Vickrey BG, Passaro EA: Early and late cognitive changes following temporal lobe surgery for epilepsy. *Neurology* 60: 951-959, 2003
12) Engman E, Andersson-Roswall L, Samuelsson H, Malmgren K: Serial cognitive change patterns across time after temporal lobe resection for epilepsy. *Epilepsy Behav* 8: 765-772, 2006
13) Hermann BP, Wyler AR, Somes G: Language function following anterior temporal lobectomy. *J Neurosurg* 74: 560-566, 1991
14) Langfitt JT, Westerveld M, Hamberger MJ, et al.: Worsening of quality of life after epilepsy surgery: effect of seizures and memory decline. *Neurology* 68: 1988-1994, 2007
15) Erturk Cetin O, Isler C, Uzan M, Ozkara C: Epilepsy-related brain tumors. *Seizure* 44: 93-97, 2017
16) Giulioni M, Marucci G, Martinoni M, et al.: Epilepsy associated tumors: review article. *World J Clin Cases* 2: 623-641, 2014
17) Chan CH, Bittar RG, Davis GA, Kalnins RM, Fabinyi GC: Long-term seizure outcome following surgery for dysembryoplastic neuroepithelial tumor. *J Neurosurg* 104: 62-69, 2006
18) Hitiris N, Mohanraj R, Norrie J, Sills GJ, Brodie MJ: Predictors of pharmacoresistant epilepsy. *Epilepsy Res* 75: 192-196, 2007
19) Wechsler D: Manual for the Wechsler Memory Scale-Revised. San Antonio, TX, The Psychological Corporation, 1987
20) Luyken C, Blumcke I, Fimmers R, et al.: The spectrum of long-term epilepsy-associated tumors: long-term seizure and tumor outcome and neurosurgical aspects. *Epilepsia* 44: 822-830, 2003
21) Kadish NE, Bast T, Reuner G, et al.: Epilepsy surgery in the first 3 years of life: predictors of seizure freedom and cognitive development. *Neurosurgery* 84: E368-E377, 2019
22) Forthoffer N, Brissart H, Tyvaert L, Maillard L: Long-term cognitive outcomes in patient with epilepsy. *Rev Neurol (Paris)* 176: 448-455, 2020
23) Spencer S, Huh L: Outcomes of epilepsy surgery in adults and children. *Lancet Neurol* 7: 525-537, 2008
24) Kwan P, Brodie MJ: Neuropsychological effects of epilepsy and antiepileptic drugs. *Lancet* 357: 216-222, 2001
25) Helmstaedter C, Elger CE, Witt JA: The effect of quantitative and qualitative antiepileptic drug changes on cognitive recovery after epilepsy surgery. *Seizure* 36: 63-69, 2016
26) Oyegbile TO, Dow C, Jones J, et al.: The nature and course of neuropsychological morbidity in chronic temporal lobe epilepsy. *Neurology* 62: 1736-1742, 2004
27) Jokeit H, Ebner A: Effects of chronic epilepsy on intellectual functions. *Prog Brain Res* 135: 455-463, 2002
28) Holthausen H, Blumcke I: Epilepsy-associated tumours: what epileptologists should know about neuropathology, terminology, and classification systems. *Epileptic Disord* 18: 240-251, 2016
29) Blumcke I, Aronica E, Urbach H, Alexopoulos A, Gonzalez-Martinez JA: A neuropathology-based approach to epilepsy surgery in brain tumors and proposal for a new terminology use for long-term epilepsy-associated brain tumors. *Acta Neuropathol* 128: 39-54, 2014
30) Siegel RL, Miller KD, Jemal A: Cancer statistics, 2019. *CA Cancer J Clin* 69: 7-34, 2019
31) Sandberg DI, Ragheb J, Dunoyer C, Bhatia S, Olavarria G, Morrison G: Surgical outcomes and seizure control rates after resection of dysembryoplastic neuroepithelial tumors. *Neurosurg Focus* 18: E5, 2005
32) Bonney PA, Boettcher LB, Conner AK, et al.: Review of seizure outcomes after surgical resection of dysembryoplastic neuroepithelial tumors. *J Neurooncol* 126: 1-10, 2016
33) Slegers RJ, Blumcke I: Low-grade developmental and epilepsy associated brain tumors: a critical update 2020. *Acta Neuropathol Commun* 8: 27, 2020
34) Morris HH, Matkovic Z, Estes ML, et al.: Ganglioglioma and intractable epilepsy: clinical and neurophysiologic features and predictors of outcome after surgery. *Epilepsia* 39: 307-313, 1998
35) Elwood RW: The Wechsler Memory Scale-Revised: psychometric characteristics and clinical application. *Neuropsychol Rev* 2: 179-201, 1991
36) Bornstein RA, Chelune GJ: Factor structure of the Wechsler Memory Scale-revised in relation to age and educational level. *Arch Clin Neuropsychol* 4: 15-24, 1989

Corresponding author: Nobuhiro Mikuni, M.D., Ph.D.
Department of Neurosurgery, Sapporo Medical University, South1 West16, Chuo-ku, Sapporo, Hokkaido 060-8543, Japan.
e-mail: mikunin@sapmed.ac.jp