Contralateral Hippocampal Stimulation for Failed Unilateral Anterior Temporal Lobectomy in Patients with Bilateral Temporal Lobe Epilepsy

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Key Words

Anterior temporal lobectomy · Bilateral temporal lobe epilepsy · Deep brain stimulation

Abstract

Aims: To prospectively study the surgical outcomes of unilateral anterior temporal lobectomy (ATL) in patients with intractable bilateral temporal lobe epilepsy (TLE) as well as two-staged contralateral hippocampal stimulation in patients after failed unilateral ATL. **Methods:** Eighteen carefully selected patients with bilateral TLE underwent unilateral ATL. Five cases with failed ATL underwent two-staged contralateral hippocampal stimulation. Seizure control and changes in intelligence quotient (IQ), memory quotient, and quality of life (QOL) were analyzed 2–5 years after treatment. **Results:** In the patients with unilateral ATL, the percentages seizure free were 55.6% (10/18), 50.0% (9/18), and 44.4% (4/9) at the 1-, 2-, and 5-year follow-up visits, respectively. There was significant difference in seizure control between the patients with unilateral ATL and the 12 cases in the medication group. Significant differences were also found in changes in the patients' QOL and full-scale IQ at the 2-year follow-up between the surgical and medication groups. Five patients who underwent contralateral hippocampal stimu-

lation after failed unilateral ATL experienced 80–100% seizure reductions, and 80% were seizure free 1 year after hippocampal stimulation. **Conclusion:** Unilateral ATL provides good seizure control and does not cause serious memory or IQ injury in carefully selected patients with true bilateral TLE. Contralateral hippocampal stimulation is a useful approach for patients who experience unilateral ATL failure.

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Introduction

Intractable seizures are defined as seizures that persist despite therapy with modern anticonvulsants at adequate serum levels [1]. Surgical intervention is a safe and effective approach for patients with epilepsy who exhibit medically intractable seizures. Seizures arising from mesial temporal structures such as the amygdala, hippocampus, and parahippocampal gyrus occur in more than 90% of patients with temporal lobe epilepsy (TLE) and are most commonly ameliorated by anterior temporal lobectomy (ATL) [2].

It is known that patients with independent spikes or sharp waves over the bilateral temporal regions do not obtain as high a rate of complete seizure control after

Table 1. Inclusion criteria

1	Subjects who had their epilepsy treated by more than 2 types of AEDs for at least 2 years, with no fewer than 12 unprovoked complex partial seizures with or without a secondary generalized seizure in the last 3 months
2	IQ >50, 10–40 years old, male or female
3	Seizure semiologies were in accordance with an origin in the temporal lobe and included at least 2 types of semiologies
4	Subjects whose MRI scan revealed unilateral or bilateral hippocampal sclerosis
5	Subjects whose recent interictal EEG showed bilateral or predominantly unilateral anterior temporal spike discharge during the interictal period
6	Subjects whose scalp and intracranial EEGs uncovered independent bilateral mesial temporal lobe rhythmic activity during the ictal period and unilateral epileptiform discharges during seizure onset with corresponding seizure semiology, such as ipsilateral upper limb automatism, contralateral head inversion, or tonic limbs
7	PET revealed bilateral or unilateral temporal lobe hypometabolism
8	Subjects without progressive neurological diseases
9	Subjects who did not exhibit extratemporal lobe involvement in a comprehensive preoperative assessment
10	Over 2/3 seizure onsets in 1 ipsilateral temporal lobe during intracranial EEG monitoring

temporal lobe surgery compared with patients with a unilateral temporal lobe focus [3–5]. The prognostic significance of unilateral temporal spikes in the scalp electroencephalogram (EEG) as a predictor of outcome after temporal lobe surgery has been reinforced by several studies [6, 7]. However, interictal spikes or sharp waves over the bilateral temporal region are not rare [8–10], and autopsies of chronically institutionalized patients with clinical diagnoses of TLE have provided a spectrum of bilateral temporal pathology, with evidence of some type of bilateral temporal pathology in as many as 80% of patients and bilateral hippocampal sclerosis in 50% [11]. Furthermore, not all patients with bilateral temporal spikes experience poor seizure control, and approximately 54% become seizure free after surgery [3].

However, some patients with epilepsy suffer truly bilateral TLE, who present independent bilateral temporal epileptogenic foci, and how to treat these patients remains controversial. The most pertinent concern about bilateral TLE arises from the fact that independent bilat-

eral temporal seizures can cause surgery to fail, as after the resection of one temporal lobe seizures sometimes continue to arise from the other lateral side [2–4]. This phenomenon has caused controversy over whether contralateral hippocampal stimulation should be taken into consideration after the failure of unilateral ATL. In this study, we investigated the outcome of operations in patients with bilateral TLE.

Methods

Patients

This prospective study on unilateral ATL included 10- to 45-year-old patients who were suffering from bilateral TLE. Those patients were treated from September 2004 to December 2012 and had finished 3 years of follow-up with detailed clinical data. All of the patients were diagnosed with bilateral TLE in accordance with the inclusion criteria list shown in table 1. The multidiscipline specialist team of the Capital Epilepsy Therapy Center in Beijing performed the diagnoses. The investigation was approved by the ethics committees of the First Affiliated Hospital of PLA General Hospital in May 2004. Those patients who refused surgery after the detailed introduction of surgery by doctors for bilateral TLE were placed into the medication group; those patients who underwent ATL were placed into the surgery group. This prospective study on contralateral hippocampal stimulation included patients who suffered continuous seizure after unilateral ATL in the previous study and were willing to undergo contralateral hippocampal stimulation. This investigation was approved by the ethics committees of the First Affiliated Hospital of PLA General Hospital in July 2013.

Preoperative Assessments

Preoperative evaluations included a neurological assessment, long-term video-EEG recording, magnetic resonance imaging (MRI), 2-deoxy-2-[¹⁸F]-fluoro-D-glucose-positron emission tomography (FDG-PET), and neuropsychological tests. The scalp video-EEG was recorded by a 64-channel recorder, and the recordings were completed after the gradual withdrawal of AEDs over 3–5 days. At least 6 seizures and 2 types of semiologies were recorded by the video-EEG. The MRI scan included axial T1 and T2 fluid attenuation inverse recovery and diffusion-weighted imaging, sagittal T1-weighted imaging, and coronal hippocampal fluid attenuation inverse recovery imaging. FDG-PET imaging was performed after the patient had been fasting for 12 h, dieting for 24 h, and seizure free for 24 h. The Wechsler Adult Intelligence Scale (Chinese version) was used in the intelligence quotient (IQ) tests, which included verbal IQ (VIQ), performance IQ, and full-scale IQ (FIQ). The neuropsychological tests included FIQ, VIQ, and performance IQ on the Wechsler Intelligence Scale (Chinese revision; WIS-CR), the total memory quotient (MQ) test, including the digit scan, logical memory, and visual reproduction subtests in the Wechsler Memory Scale (Chinese revised version), and the overall quality of life (QOL) subscale on the Epilepsy Inventory-31 (QOLIE-31). Intracranial electrode EEG and the hemisphere anesthesia test (Wada test) were completed on all patients in the surgery group [12].

Fig. 1. MRI after hippocampal DBS. This figure shows the position of the electrode. The electrode was inserted along the longitudinal of the hippocampus, and the first contact of the electrode rested in the junction of the amygdala and hippocampus (**a**), while the second to fourth contacts lay in the basal area of the hippocampus and near the parahippocampal gyrus (**b**).

Treatment Procedure

Medication was provided to all of the patients, with 2–3 types of optimal antiepileptic drugs provided to the medication group or 1–3 types of antiepileptic drugs provided to the postoperative patients in the surgery group. All of the patients underwent unilateral ATL in the surgery group. ATL was performed on the side responsible for at least 2/3 of the seizure onsets during intracranial EEG recording. The resected cortical regions encompassed 4–5 cm on the left side and 5–6 cm on the right side of both the superior temporal gyrus and the inferior temporal gyrus. At least 3–4 cm of the hippocampus was removed.

Contralateral hippocampal stimulation was performed on those patients who suffered more than 4 seizures per month 1 year after unilateral ATL and did not exhibit extratemporal lobe involvement during an additional comprehensive preoperative assessment. Under general anesthesia and in a prone position, a stereotaxic head frame was used to insert a quadripolar electrode 1.5 mm in length with an interelectrode distance of 1.5 (PINZ-L302; Pinz Inc., Beijing, China) along the hippocampal axis such that that the first contact of the electrode rested in the junction of the amygdala and hippocampus, and the second to fourth contacts remained in the basal area of the hippocampus and near the parahippocampal gyrus (fig. 1).

Follow-Up

All of the patients were evaluated 1, 2, and 5 years (if possible) after treatment. A postoperative assessment, including surgical outcomes and complications, was completed at these visits. The surgical outcomes were expressed as changes in the IQ, MQ, and QOL scores and the reduction in seizure frequency. The postoperative IQ, MQ, and QOL were tested at the 2-year follow-up. Cut-off values for postoperative to preoperative changes in IQ, MQ, and QOL were 10% and –10% of the preoperative scores. The seizure reduction was determined by comparing the seizure frequency during the 12 months prior to each follow-up visit with the baseline seizure frequency. The seizure control outcomes were classified into class I (seizure free), class II (rare seizures), class III (>90% reduction in seizure frequency), or class IV (<90% reduction in seizure frequency) according to the Engel method. The patients were divided into a favorable seizure control group (Engel class I–II) and unsatisfactory groups (Engel class III–IV) to determine

the predictor for favorable seizure control. Complications were described as transient or permanent. Nurses in the hospital recorded transient complications in the 2 weeks following surgery, while caregivers registered permanent complications 2 weeks to 12 months after the operation.

Statistical Analysis

Statistical analyses were completed with the SPSS statistical program (version 18.0; SPSS, Inc., Chicago, Ill., USA). The outcomes were described with percentages, means, and standard deviations. χ^2 and Fisher's exact tests were carried out for univariate analyses of categorical variables. The t test and F test were used to compare quantitative data. p values <0.05 were considered significant.

Results

Presurgical Data for All Patients

The demographics and preoperative data for the 30 patients are provided in online supplementary table 1 (see www.karger.com/doi/10.1159/000449008 for all online suppl. material). Twelve patients were grouped into the medication group. Eighteen patients underwent ATL, including 5 patients who received contralateral hippocampal stimulation and unilateral ATL. The average age at seizure onset was 10.00 ± 4.98 years (range: 1.5–16) in the surgery group and 11.25 ± 6.55 years (range: 1–25) in the medication group. The average age at treatment in our hospital was 24.72 ± 7.28 years (range: 10–39) in the surgery group and 23.92 ± 6.47 years (range: 15–31) in the medication group. The age, gender, side of hippocampal sclerosis, cause of epilepsy, preoperative FIQ, score of overall QOL, and total score of MQ of the surgery group and the medication group did not differ significantly (table 2). All patients in the surgery group

Table 2. Surgical outcome at 2-year follow-up in patients with unilateral ATL

	Preoperative scores			Changes			Seizure control		Percentage of satisfaction
	QOL	FIQ	Total MQ	QOL	FIQ	Total MQ	I-II	III-IV	
<i>Group</i>									
Medicine	59.92±7.79	72.08±13.58	66.08±15.80	-2.17±3.44 ^{##}	-2.08±2.56 [#]	-1.50±2.06 [#]	1 [#]	11	61.13±10.34 ^{##}
Surgery	60.56±9.22	75.61±15.79	69.67±18.19	5.67±6.11	3.22±5.69	0.94±3.33	11	7	80.50±17.07
<i>Seizure control</i>									
I-II	59.18±7.13	74.55±13.72	74.46±15.42	9.73±3.32 ^{**}	6.91±3.08 ^{**}	2.18±3.06	11 ^{**}	0	93.00±4.56 ^{**}
III-IV	62.71±12.13	77.29±19.69	62.14±20.80	-0.71±3.09	-2.57±3.46	-1.00±2.94	0	7	60.86±7.36
<i>Side of ATL</i>									
Right	63.10±9.23	82.20±14.39	77.40±17.54	7.50±5.15	5.40±5.36	2.90±1.67 ^{**}	7	3	85.60±14.61
Left	57.38±8.72	67.38±14.14	60.00±14.68	3.96±6.76	1.488±5.15	-0.74±3.34	4	4	74.13±18.70
<i>Duration of seizure</i>									
≤10 years	60.50±8.24	77.80±13.98	72.90±12.00	9.50±4.03 ^{**}	6.90±2.81 ^{**}	1.50±3.84	9 ^{**}	1	90.20±12.73 ^{**}
>10 years	60.63±10.91	72.88±18.42	65.63±27.17	0.88±4.73	-1.38±5.01	0.25±2.66	2	6	68.38±14.03
<i>Age at surgery</i>									
≤25 years	58.46±8.55	73.64±12.48	67.27±14.42	6.73±6.45	4.18±5.83	0.91±3.78	8	3	83.55±17.40
>25 years	63.86±9.91	78.71±20.70	73.43±23.73	4.00±5.57	1.71±5.56	1.00±2.77	3	4	75.71±16.64
<i>Etiology of TLE</i>									
FC	60.86±9.05	76.14±15.84	71.14±21.37	5.14±6.57	3.28±6.04	0.29±3.63	4	3	78.29±18.25
Encephalitis	59.80±9.04	74.20±18.27	62.40±22.33	3.00±6.63	-0.20±6.26	0.60±2.60	2	3	75.00±19.42
Unknown	60.83±11.16	76.17±16.65	74.00±9.96	8.50±4.76	6.00±3.74	2.00±3.79	5	1	87.67±13.79
<i>Hippocampus sclerosis</i>									
Bilateral	61.63±9.59	78.00±17.87	65.13±17.83	3.75±6.94	1.13±6.13	0.88±2.53	3	5	76.63±18.09
unilateral	59.43±8.58	74.29±13.76	77.86±15.55	10.00±2.58	7.00±2.94	3.29±1.80	7 [*]	0	91.43±3.74 [*]
No	60.33±13.05	72.33±19.73	62.67±24.13	0.67±3.21	0.00±5.20	-4.33±1.15 ^{**}	1	2	65.33±21.57

Changes: changes in the score from preoperative to the 2-year follow-up visit (postoperative score minus preoperative score). FC = Febrile convulsive. [#] p < 0.05, ^{##} p < 0.01, change in the medicine group compared with change in the surgery group. ^{*} p < 0.05, ^{**} p < 0.01, change in this group compared with changes in the other group with the same effect factor.

underwent intracranial EEG examination, including 4 stereotactic EEG and 14 depth electrodes with strip electrode EEG.

Seizure Control after Unilateral ATL

The seizure control outcomes are listed in table 2. In the patients with unilateral ATL, 55.6% (10/18) were seizure free at the 1-year follow-up, 50.0% (9/18) were seizure free at the 2-year follow-up, and 44.4% (4/9) were seizure free at the 5-year follow-up, with 11.1% (2/18), 11.1% (2/18), and 11.1% (1/9) of patients reaching Engel grade II at the 1-, 2-, and 5-year follow-up visits, respectively. However, the percentage of patients achieving favorable seizure control (Engel I-II) in the medication group was 16.7 and 8.3%, respectively, at the 1- and 2-year follow-up visits and 0% at the 5-year follow-up. A higher percentage of patients in the surgery group achieved favorable seizure control (Engel I-II) than the medication group at all three follow-up visits, and there was a signif-

icant difference in seizure outcome between the two groups at all follow-up visits. The patients with a short (<10 years) preoperative seizure history made up a significantly higher percentage of the patients with favorable seizure control than those patients with a long preoperative seizure history, and patients with unilateral hippocampus sclerosis had significantly better seizure control than those patients with bilateral hippocampus sclerosis and without hippocampus sclerosis. However, there were no significant differences in age at surgery, etiology, side of ATL, and preoperative FIQ between those patients with class I-II seizure control and those with unsatisfied seizure control 2 years after unilateral ATL (table 2).

Changes in QOL, IQ, and MQ, and Patient Satisfaction at the 2-Year Follow-Up

All of the patients' pretreatment overall QOL, FIQ, and total MQ scores and changes from pre- to posttreatment scores are listed in table 2 and online supplemen-

Table 3. Demographic and clinical data of patients with hippocampal stimulation

Patient No.	Sex	Age at first seizure, years	Age at ATL, years	History of seizure, years	Cause	Hippocampal stimulation on MRI	Side of ATL	Hip-DBS time after ATL, months	Side of Hip-DBS	Stimulus parameters		
										voltage, V	frequency, Hz	wave width, μ s
14	M	5	35	30	Encephalitis	Bilateral	Right	27	Left	1.9	130	300
15	M	1.5	10	8.5	FC	No	Left	24	Right	2.2	130	450
16	F	5	39	34	Unknown	Bilateral	Right	24	Left	2.0	130	300
17	M	4	31	27	FC	Bilateral	Left	26	Right	1.0	130	300
18	F	5.5	34	28.5	Encephalitis	Bilateral	Right	25	Left	1.6	130	300

FC = Febrile convulsive.

tary table 1. When the postoperative scores for the overall QOL, FIQ, and total MQ were compared with the preoperative scores for each child, there were 14 patients (77.8%, including 9 with postoperative changes $\geq 10\%$ of the preoperative score) with a postoperative QOL improvement and 4 (22.2%) decreases in the ATL group, with 3 (25%) and 7 (58.3%) in the medication group, respectively. There were 12 patients (66.7%, including 7 with postoperative changes $\geq 10\%$ of the preoperative score) with a postoperative FIQ improvement, and 5 (27.8%) decreases were found compared with preoperative scores in the ATL group, with 3 (25%) and 9 (75%) in the medication group, respectively. There were 11 patients (66.7%, none with postoperative changes $\geq 10\%$ of the preoperative score) with postoperative full-scale MQ improvement and 5 (27.8%) decreases in the ATL group, with 3 (25%) and 8 (66.7%) in the medication group, respectively. Furthermore, the improvement in MQ, QOL, and IQ reached 10% of preoperative scores in none of the patients in the medication group, while 1 QOL decrease (8.3%), 1 IQ decrease (8.3%), and 1 postoperative MQ decrease (8.3%) were $>10\%$ of preoperative scores. Significant differences were found in changes of QOL, IQ, and MQ between the ATL group and the medication group ($p < 0.05$).

The average overall QOL score improved by 5.67 in the surgery group and was significantly higher than the -0.92 experienced in the medication group ($p = 0.0016$) (table 3). There were also significant differences in the change in FIQ and MQ ($p = 0.0020$) and the percentage of patients satisfied with treatment between the surgery group and the medication group. Furthermore, the percentage of satisfaction for ATL and improvements in overall QOL and FIQ, but not MQ, were significantly

higher in those patients who exhibited favorable postoperative seizure control and a short preoperative seizure history than in those with poor postoperative seizure control and a long preoperative seizure history. However, the improvement in postoperative full-scale MQ was significantly higher in patients with right ATL than those with left ATL (table 2), patients with unilateral hippocampus sclerosis than those with bilateral hippocampus sclerosis and without hippocampus sclerosis, and patients with normal preoperative IQ than those with low preoperative IQ. Also, those cases with favorable seizure control, short preoperative seizure history, and unilateral hippocampus sclerosis rendered significant high patient satisfaction.

Surgical Outcomes of Unilateral ATL Combined with Contralateral Hippocampal Stimulation

Patients 14 and 16 underwent left hippocampal stimulation 27 and 24 months after right ATL, respectively, and presented seizure free at the 2-year follow-up. Patient 15 underwent right hippocampal stimulation 24 months after left ATL and achieved Engel grade II seizure control at the 2-year follow-up. Patient 17 underwent right hippocampal stimulation 26 months after the failure of left ATL and presented 3 seizures at 6 months, and 1 seizure attack in the 7–12 months of follow-up. The patient was seizure free at the 2-year follow-up. Patient 18 underwent left hippocampal stimulation 25 months after the failure of right ATL and reached Engel grade I seizure control at the 18-month follow-up. Therefore, 5 patients who underwent contralateral hippocampal stimulation after failed unilateral ATL experienced 80–100% seizure reductions, and 80% were seizure free 1 year after hippocampal stimula-

Fig. 2. Changes of seizure frequency (a), QOL (b), FIQ (c), and MQ (d) at 6 months before ATL, 24 months after unilateral ATL, and 18 months after contralateral hippocampal DBS in 5 patients (cases 14–18). All patients reached over 90% seizure reduction at the 6-month follow-up after unilateral ATL, but the seizure frequencies increased at the 18- and 24-month follow-up visits. Cases 14,

16, and 18 presented seizure free after contralateral hippocampal DBS, case 17 presented seizure free in the last year, and the other case presented Engel II class seizure control at the 2-year follow-up. -6-ATL = 6 months before ATL; ATL-6 = 6 months after ATL; DBS-6 = 6 months after hippocampal DBS.

tion. All of the cases used the continuous stimulation mode. The stimulation parameters and the patients' demographic and clinical data are list in table 3. The average postoperative QOL of the aforementioned 5 patients improved by 6.2 compared with pre-ATL data and by 5.6 compared with data before deep brain stimulation (DBS). At the same time, the average postoperative FIQ improved by 5.2 and 6.2, respectively. The changes in seizure frequency and QOL, IQ, and MQ are shown in figure 2.

Surgical Complications

None of the patients developed permanent complications. Transient complications appeared in a total of 3 cases and included 2 cases of aphasia and 1 case of apraxia after ATL. There were no complications after contralateral hippocampal stimulations.

Discussion

The diagnostic criteria for bilateral TLE are still developing. From the early stage of epilepsy surgery, bilateral TLE has been diagnosed on the basis of clinical semiology and findings from MRI and scalp EEG [6]. However, it is not rare for patients with TLE to present with bilateral temporal lobe epileptiform discharges on scalp EEG, and only 11.5% of patients were true bilateral TLE [3]. Therefore, intracranial electrode EEG is commonly used in the diagnosis of bilateral TLE, although the use of this method is not obligatory. All of the patients in our cohort, whether exhibiting bilateral hippocampal sclerosis or unilateral hippocampal sclerosis, were diagnosed with bilateral TLE according to the results of bilateral intracranial electrode EEG, and they all exhibited unilateral epileptiform discharges at the onset of each seizure with the corresponding seizure semiology, such as ipsilateral upper limb automatism, contralateral head version, or tonic limbs [13]. We em-

phasize the consistency in the ictal epileptiform discharge pattern and seizure semiology in the diagnosis of bilateral TLE. Last and most importantly, it was not uncommon to find patients with extratemporal epileptogenic foci with misleading clinical or EEG features falsely localizing to the bilateral temporal lobe. Therefore, the diagnosis of bilateral TLE must be built after the exclusion of extra-TLE.

Unilateral ATL is the most commonly utilized surgery in patients with bi-TLE. However, the seizure control outcomes after this surgery are varied. Holmes et al. [14] reported 19 cases with bilateral TLE, with 6 (31.6%) presenting Engel level I–II seizure control after ATL. On the other hand, Loesch et al. [13] performed unilateral ATL in 11 patients with bilateral TLE, with 10 (90.9%) achieving postoperative Engel level I–II seizure control, and Cukiert [15] reported that all 9 patients with bilateral TLE who received unilateral ATL attained Engel level I–II seizure control 5–10 years after the procedure. Aghakhani et al. [3] reviewed 1,403 patients with ambiguous or presumed bilateral TLE on scalp EEG, determining that 1,027 (73%) exhibited unilateral TLE on intracranial EEG and underwent unilateral ATL. Of these patients, 58% achieved Engel class I control, and 9% achieved an Engel class II outcome. Overall, 173 of the patients exhibited true bilateral TLE, with 33 and 15% achieving Engel class I and II outcomes after unilateral ATL, respectively. In our cohort, 59% of patients achieved favorable seizure control at the 1-year follow-up, 53% exhibited favorable seizure control at the 2-year follow-up, and 45% showed favorable seizure control at the 5-year unilateral ATL follow-up visit. In contrast, none of the patients receiving medication exhibited favorable seizure control at the 5-year follow-up. Although there were no significant differences in seizure onset laterality on intracranial EEG (the proportion of seizures ipsilateral to the resection) between the patients with good (76%, range: 42–95%) or poor outcomes (78%, range: 50–97%; $p = 0.68$) [3], most of the reported patients with bilateral TLE and unilateral ATL present with over 70% seizure onset laterality, as in this study. The resection of the dominant epileptogenesis zone combined with the administration of postoperative AEDs can result in favorable seizure control [16]. Therefore, unilateral ATL is an efficient approach for seizure control in bilateral TLE, although this approach is more effective in patients with unilateral TLE [3, 17–19].

Because patients with bilateral TLE often exhibit bilateral temporal lobe injury, the Wada test must be examined before unilateral ATL in these patients [12]. Those

patients who underwent ATL exhibited improved QOL and intelligence scores compared with the preoperative scores, with the patients experiencing favorable postoperative seizure control exhibiting the greatest improvements. In our cohort, memory injury is significantly more in patients with ATL on the dominant side and ATL in bilateral TLE without hippocampus sclerosis than in those with ATL on the right side or bilateral TLE without hippocampus sclerosis. Of 8 patients with left ATL, there were 5 cases who presented memory decrease; however, the MQ decrease reached 10% of the preoperative score in none of this cohort. The reasons serious MQ injury was prevented included 3 aspects: first, the Wada test was performed, and short-term memory was accessed during the Wada test in every patient; second, the patients with obvious memory injury during the Wada test were excluded from unilateral ATL in patients with bilateral TLE; third, the resection region of dominant-side ATL was strictly limited to 3.5 cm of neocortex and 2 cm of hippocampus from the temporal lobe polar. In contrast, the QOL and IQ scores for those patients receiving medication therapy decreased. Thus, the concerns about postoperative decreases in QOL, memory, and intelligence might be unnecessary in patients with bilateral TLE when the preoperative Wada test indicates the safety of unilateral ATL.

Hippocampal stimulation is another approach for the treatment of TLE. We reviewed the cases of 49 patients with TLE who underwent hippocampal stimulation [20–23] (unpublished material). Eighteen percent of these patients achieved seizure-free status, while 55.1% exhibited a 50% reduction in seizures. Of the 30 patients who underwent unilateral hippocampal stimulation, 73.4% achieved a 50–100% reduction in seizures. In this cohort, 5 patients with failed unilateral ATL and bilateral TLE underwent contralateral hippocampal stimulation and achieved promising outcomes. Four patients with bilateral hippocampus sclerosis and bilateral TLE became seizure free, and the patient with bilateral TLE without hippocampus sclerosis presented continuous postoperative seizures. Our result was contradictory to a previous study, which showed that hippocampal DBS rendered favorable seizure control in patients without hippocampus sclerosis, but this study did not combined first-stage unilateral ATL [24]. Therefore, unilateral ATL and two-staged contralateral hippocampal stimulation in patients could be a useful approach for bilateral TLE with hippocampus sclerosis.

Conclusion

Unilateral ATL attained favorable seizure control and neuropsychology improvements without affecting the QOL of carefully selected patients with bilateral TLE. Second-stage contralateral hippocampal stimulation is a promising approach for patients with bilateral TLE and failed unilateral ATL. However, more investigation into this combined therapeutic approach for bilateral TLE is necessary.

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Author Contributions

D.P. and L.S. designed the study, performed the operations, and drafted the manuscript. Z.S. and Z.J. were responsible for patient management and participated in its design and operation. H.X. participated in patient management and drafted the manuscript. G.C. and L.S. participated in the design of the study and performed the statistical analysis. Y.X. was in charge of the program control of the DBS and the collection of patient information. All authors read and approved the final manuscript.

Disclosure Statement

The authors declare that they have no competing interests.

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