Anterior temporal lobectomy combined with anterior corpus callosotomy in patients with temporal lobe epilepsy and mental retardation

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A B S T R A C T

Aims: To investigate the surgical outcomes of anterior corpus callosotomy (aCCT) combined with anterior temporal lobectomy (ATL) in patients with intractable temporal lobe epilepsy (TLE) and mental retardation (MR).

Methods: Sixty patients with TLE and MR were carefully selected and randomly divided into two equal groups: ATL and aCCT, in which they were treated with ATL or ATL combined with aCCT, respectively. Surgical outcomes, including seizure control, IQ and quality of life (QOL) changes, as well as complications were recorded and analyzed 2 years after operation.

Results: Seizure-free status had been achieved in 66.7% of all patients. The aCCT group had higher percentage in Engel Classes I–II than the ATL group (96.7% vs. 80.0%, P < 0.05). 56.7% of patients in ATL group and 63.3% in aCCT group had improved full scale IQ (FIQ) after surgery, while the decline of FIQ in aCCT group was less than that of ATL group (3.3% vs. 30.0%). Compared with pre-operative score, the mean post-operative score of performance IQ in aCCT group had improved. Significant difference in QOL change had been found between two groups (P < 0.001). 73.7% of patients in aCCT group had their QOL improved with no long-term complications.

Conclusions: ATL combined with aCCT can improve QOL and performance IQ in patients with TLE and MR.© 2010 British Epilepsy Association. Published by Elsevier Ltd. All rights reserved.

1. Introduction

Mental retardation (MR), defined as Wechsler Full Scale Intelligence Quotient (FIQ) ≤70, is an important comorbidity of chronic epilepsy.1 MR is found in 38–49% of children and in 23% of adult with active epilepsy. MR is even more common in patients with intractable epilepsy.2,3 For patients with severe epilepsy and MR who failed to respond to anti-epileptic drugs (AEDs), they should beware that surgical intervention is also available as current epilepsy treatment in addition to medicine therapy. Although low IQ had been considered as a contraindication to epileptic surgery for a long time, Gleissner et al. recently stated that pre-operative IQ had no effects on post-operative prognosis.4 At the same time, other researchers showed that patients with pre-operative low IQ had higher risk of continued seizure compared with those with normal IQ. But low IQ should not be considered as the independent predictor of seizure outcome, and many low-IQ patients had benefited from the epileptic surgery. Therefore, patients with low IQ should not be excluded from epileptic surgery.5,6 Resective surgery4,6 and palliative surgery, which included corpus callosotomy (CCT)7,8 and vagus nerve stimulation,9 have been adopted for those patients. Anterior temporal lobectomy (ATL) is a standard procedure of temporal lobe epilepsy (TLE), which is the most common type of epilepsy for surgery, and it has been used for patients with partial epilepsy and MR. About 33–48% of patients with MR were seizure-free following ATL.4,6 Whereas in patients with normal IQ, the rate was 66–75%.10 The difference may have been resulted from structural and functional cerebral changes in patients with MR.11

CCT was introduced in 1940 by Van Wagenen and Herren. This technique included anterior corpus callosotomy (aCCT), posterior CCT, one-stage or two-stage total CCT, and the recently developed radiosurgical CCT with gamma knife7. It had successfully overcome a wide variety of seizures and epilepsy syndromes, and had been accepted as a palliative surgical procedure for some patients with intractable seizures including intractable generalized epilepsy and severe epilepsy with multiple independent epileptogenic foci. Satisfactory outcome could be achieved in 85% patients that had drop attacks and 62% patients had their daily function improved.12 It had been used for patients with partial epilepsy and the outcome...
had been promising. Others reported that CCT could improve quality of life (QOL) and IQ of epileptic patients.

We made an assumption that ATL combined with aCCT may improve surgical outcome for patients with TLE and MR, hence carried out this prospective comparative study.

2. Patients and methods

2.1. Patients

The trial commenced in January 2003 and ended in September 2006. Sixty patients with intractable TLE were involved in the trial and were divided equally into two groups. Final results were concluded in September 2008. Patients were enrolled in this trial according to the criteria listed in Table 1. Dr. Liang and Dr. Zhao introduced the trial to their families. Sixty patients, who had their family members signed the consent form and agreed to accept ATL or ATL combined with aCCT, were numbered from 1 to 60. Patients were divided into two groups according to odd-even and the groups were named ATL group and aCCT group, respectively.

2.2. Pre-operative assessments

Pre-operative evaluations included neurological assessment, long-term video-electroencephalogram (EEG) recording, magnetic resonance imaging (MRI), 2-deoxy-2\(^{18}\)F fluoro-D-glucos-positron emission tomography (FDG-PET) and IQ test. Scalp Video-EEG was recorded by 64 channels recorder, and the recordings had been performed after gradual withdrawal of AEDs. There were at least three seizures recorded by Video-EEG. MRI scan included axial T1, T2, fluid attenuation inverse recovery (FLAIR) and diffusion-weighted imaging, sagittal T1-weighted imaging and coronal hippocampus FLAIR imaging. FDG-PET examination was performed after the patient had been fasting for 12 h, dieting for 24 h and seizure-free for 24 h. IQ tests were performed with the Wechsler Child Intelligence Scale (Chinese version) in children from 6 to 16 years old and with the Wechsler Adult Intelligence Scale (Chinese Version) in other patients. IQ included verbal IQ (VIQ), performance IQ (PIQ) and full scale IQ (FIQ). All of the patients were included into the study by the multidiscipline specialist team of Capital Epilepsy Therapy Center in Beijing.

2.3. Surgical procedure

Patients in ATL group were treated with ATL and patients in aCCT group were treated with ATL combined with aCCT. Standard procedure had been used in ATL group. Resective regions included 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 2–3.5 cm hippocampus had been removed. When aCCT was combined with ATL, unique incision on both fronto-temporal flap and bone flap were needed. The aCCT was performed after ATL. The callosotomy should be performed from posterior to anterior extent of resection, following full exposure of the posterior part of the corpus callosum where callosotomy was planned to be done. The anterior extent of resection was defined by the dorsal surface of the anterior cerebral arteries. The corpus callosum had been disconnected until ependyma was visible. It was important to extend the resection through all commissural fibers. The callosotomy was performed under microscope. According to different age groups, the length of dissection was 6–7 cm, which was about 2/3 of corpus callosum.

2.4. Follow-up

All of the patients were evaluated at 2-year follow-up visit. Post-operative assessment, including surgical outcomes and complications, was completed by Dr. Jiang and Dr. Sun. Surgical outcomes included changes in IQ, QOL and reduction in seizure frequency. Post-operative VIQ, PIQ and FIQ were checked according to the same scale as that used before surgery. Patients were classified as having “improvement”, “no change”, and “impairment” based on their relative score changes. Cutoff values for changes in IQ post-operative to pre-operative were +4 and −2. Though we did not have a commonly used tool to measure QOL of Chinese patients with epilepsy and MR, we designed a questionnaire, which had been used for more than 5 years in our center, to assess the behavioral changes of QOL (see Table 2). This questionnaire included four aspects of behavior, and each aspect contained two questions. Each question scored −2 to 2 points from “very bad” to “very good” accordingly, so overall score was −16 to 16. The questionnaire was performed by psychologists and caregivers of patients. Cutoff values for overall QOL changes post-operative to pre-operative were +2 and −2, respectively. Changes of seizure frequency were obtained based on the comparison on frequency of seizures over the last year before follow-up and it in 1 year before surgery, and classified into Class I (seizure free); Class II (rare seizures), Class III (>90% reduction in seizure frequency), and Class IV (<90 reduction in seizure frequency) according to Engel. In addition, Class I was not subdivided because it often became impossible for patients with MR to report auras. Complications were described as transient or permanent. Transient complications were recorded by nurses in hospital, and permanent complications were recorded by caregivers.

2.5. Statistical analysis

The outcomes were described by percentage, means and standard deviation. Quantitative data were analyzed by using t-test. Qualitative data were analyzed by using Pearson Chi-square test or Wilcoxon test.

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**Table 1**

<table>
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<tr>
<th>Inclusion criteria.</th>
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<tr>
<td><strong>1.</strong> Male or female subjects, 6–40 years old.</td>
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<td><strong>2.</strong> Subjects who had their epilepsy treated by more than two types of AEDs for at least 2 years, with no less than 12 unprovoked complexes or simple partial seizures with or without secondary generalized seizure in the last 3 months.</td>
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<td><strong>3.</strong> Seizure semiology was in accordance with the origin of temporal lobe epilepsy.</td>
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<td><strong>4.</strong> Subjects with mild or moderate MR (70 &lt; VIQ ≤ 85).</td>
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<td><strong>5.</strong> Subjects without progressive neurological diseases.</td>
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<td><strong>6.</strong> Subjects whose MRI scan revealed unilateral hippocampus sclerosis or normal image.</td>
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<tr>
<td><strong>7.</strong> Subjects whose recent EEG showed unilateral or predominantly (&gt;75%) lateralized anterior temporal spike discharge during the interictal period with ipsilateral rhythmic activity, maximal over the anterior temporal or subtemporal head region onset during ictal period.</td>
</tr>
<tr>
<td><strong>8.</strong> PET revealed ipsilateral temporal lobe hypometabolism or normal.</td>
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<tr>
<td><strong>9.</strong> Discordant localization was absent and intracranial EEG recording was unnecessary.</td>
</tr>
<tr>
<td><strong>10.</strong> Subjects who were able to follow the investigational study procedures and whose family members were willing to give written consent for the study.</td>
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</table>

List of 11 including criteria of patients for this study, including patients’ ages, pre-operative IQ, course of seizure, history of therapy, pre-operative examination and information consent form.
The demographic and pre-operative data of 60 patients were provided in Table 3. The average age at seizure onset was 3.4 years (range from 0.1 to 13 years) in aCCT group and 3.1 years (range from 0.2 to 10 years) in ATL group. Significant differences were not found among MRI or PET findings, pre-operative FIQ and demography between groups.

3. Results

3.1. Pre-surgical data

The demographic and pre-operative data of 60 patients were provided in Table 3. The average age at seizure onset was 3.4 years (range from 0.1 to 10 years) in ATL group and 3.1 years (range from 0.2 to 13 years) in aCCT group. The average age at surgery was 17.0 years (range from 6 to 29 years) in ATL group and 16.3 years (range from 0.2 to 13 years) in aCCT group. The average age at surgery was 17.0 years (range from 0.1 to 10 years) in ATL group and 3.1 years (range from 0.2 to 13 years) in aCCT group.

This eight-item questionnaire is used to test the changes of QOL 2 years after surgery by caregivers and psychologists.

3.2. Surgical outcomes

Surgical outcomes were listed in Table 4. Seizure-free status had been achieved in 66.7% (40/60) of all patients, including 60% of ATL group and 73.3% of aCCT group, respectively. Although there had been no significant difference in seizure outcome between the two groups, the aCCT group rendered higher percentage in Class I and Class II than ATL group (96.7% vs. 80.0%, P < 0.05).

There was no difference in FIQ changes between two groups. Improved FIQ were observed in 56.7% of patients from ATL group and 63.3% from aCCT group after surgery. However, FIQ of patients in aCCT group reduced less than that of patients in ATL group. Reduction of FIQ was found in only 3.3% of patients in aCCT group after surgery, meanwhile reduction of FIQ was observed in 30.0% of patients in ATL group. Compared with pre-operative score, post-operative mean score of VIQ, PIQ and FIQ raised in both groups (see Table 5). However PIQ in aCCT group was the only one matched the definition of significant improvement (>4 points) and improved 5.17 points on average. Significant difference in QOL was found in both groups (P < 0.001), especially 73.7% of patients in aCCT groups had QOL improved. As shown in Table 6, patients in ATL group had less improvement in daily living (P < 0.05), movement (P < 0.001) and abnormal behavior compared with aCCT group, and their learning abilities improved the least in all aspects of QOL in aCCT group.

3.3. Complications

In all patients, there were no permanent complications developed. Transient complications appeared in nine cases in total, including two cases of urinary incontinence, one case of unexpected action, one case of abnormal behavior, one case of abnormal mood, and five cases of movement.

This table is used to compare the difference in seizure outcome, and change of FIQ and overall QOL between aCCT group and ATL group at 2 years follow-up visit. * Wilcoxon test, P < 0.01.
aphasia and two cases of apraxia in aCCT group, and two cases of aphasia and two cases of apraxia in ATL group, respectively.

4. Discussion

To our best knowledge, this research is the first prospective study on treating patients with TLE and MR by combining CCT and ATL. CCT is mainly indicated for complex partial seizures as suggested by a few papers, and satisfactory improvement had been achieved in 14–88% of patients. The current thoughts of CCT for partial seizures are limited to treating patients with frontal lobe epilepsy who presents with rapid interhemispheric transmission, which led to the fact that the patient was diagnosed as having generalized seizure attack. However, most previous researches took CCT as an exclusive surgical procedure for patients with complex partial seizure and primary generalized seizure, which were apparently different from this trial. In our cohort, patients with TLE and MR had been treated with combination of ATL and aCCT.

MR may suggest extensive brain dysfunction in those patients, therefore, surgical outcome of ATL is less satisfactory in patients with TLE and MR than those with TLE and normal FIQ, and 37–54.2% achieved seizure-free in previous studies. It had been accepted that CCT could prevent the propagation and the synchronization of seizure discharges in potential epileptogenic zone and suppress epileptic discharge generation by reducing cortical reactivity. As a combined surgical procedure, aCCT increased the percentage of seizure-free patients to 73.3%, which was higher than the 60% in our cohort and previous studies without combined CCT. In addition, only one case (3.3%) rendered Engel III-IV of seizure control in this group, and the difference was insignificant between two groups. Besides, surgical outcome in ATL group was slightly better than those in previous studies, which may be a result of more strict inclusion criteria and the exclusion of patients with discordant localization in preoperative assessments.

Patients with TLE and MR in aCCT group had QOL improved more than the ATL group after surgery, and the difference was significant: 73.3% and 33.3% respectively. By analyzing the 4 aspects of QOL, we noticed that compared to the ATL group, patients in aCCT group had considerable improvement on physical movement and abnormal behaviors (P < 0.01). The improvement of abnormal behavior was especially meaningful to patients because 29–58% of epileptic patients had behavior problem. These problems had influenced the daily lives of themselves as well as their family members considerably. Improvements on physical activity and abnormal behaviors may have resulted from blockage of abnormal nerve signal transmission between bilateral hemispheres through the corpus callosum. This had suppressed overexcited abnormal nerve signaling that were related to abnormal behavior or emotions, such as irritability, hyperactivity and attention-deficit, manic, delusion and hallucination. Consequently, the original normal nerve signal conductions that were related to depressed emotion and impaired executive functions would be activated. Patients in aCCT group showed improved mean PIQ score and they were less likely to have decreased FIQ than those in ATL group after surgery. As a conceptual framework of treatment in patients with epilepsy and MR, the purpose of treatment is not only to control seizure but also to provide more opportunities for normal intellectual development and better quality of life. Therefore, ATL combined with aCCT is a better approach for the treatment in patients with TLE and MR.

Some reports showed that total CCT was more effective. However, it remained controversial due to different results obtained from various institutions and security of anterior CCT. There were fewer complications associated with aCCT than total CCT. Any complication will be catastrophic to patients with intractable and MR because of low IQ and QOL. So aCCT, but not total CCT, was adopted in our trial. As expected, ATL combined with aCCT did not bring obvious adverse effects.

It should be noted that the questionnaire was designed by our center to evaluate the changes of QOL and was completed by caregivers. QOL score is usually tested either before or after treatment and QOL scale should be a subjective scale completed by patients. Although this questionnaire has its limitations, it can be used as a behavioral rating scale. The questionnaire also reflects some aspects of QOL and can be used in special patients with low IQ.

5. Conclusions

ATL combined with aCCT can improve QOL and PIQ of patients with TLE and MR without increased risk of surgical complications. Therefore ATL combined with aCCT can be considered as an option to treat patients with TLE and MR.

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References


Table 6

Patients’ QOL changes from pre-operative to post-operative.

<table>
<thead>
<tr>
<th>Group</th>
<th>DL</th>
<th>LE</th>
<th>MO</th>
<th>AB</th>
<th>Overall</th>
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<tbody>
<tr>
<td>ALT</td>
<td>0.73 ± 1.18</td>
<td>0.40 ± 1.33</td>
<td>0.37 ± 1.11</td>
<td>0.43 ± 1.02</td>
<td>1.93 ± 3.85</td>
</tr>
<tr>
<td>aCCT</td>
<td>1.36 ± 1.18*</td>
<td>0.56 ± 1.45</td>
<td>2.33 ± 1.42**</td>
<td>1.60 ± 0.97**</td>
<td>5.87 ± 4.35**</td>
</tr>
</tbody>
</table>

This table is used to compare the differences in changes of overall QOL and four aspects of behavior from pre-operative to 2 years follow-up visit between aCCT group and ATL group.

* P < 0.05 Score for ALT group vs. aCCT group (group t-test).

** P < 0.01 Score for ALT group vs. aCCT group (group t-test).