Selective amygdalohippocampectomy versus anterior temporal lobectomy in the management of mesial temporal lobe epilepsy: a meta-analysis of comparative studies

A systematic review

Wen-Han Hu, M.D., Ph.D.,1 Chao Zhang, M.D.,2 Kai Zhang, M.D., Ph.D.,2 Fan-Gang Meng, M.D., Ph.D.,1 Ning Chen, M.D.,2 and Jian-Guo Zhang, M.D., Ph.D.1,2

1Beijing Neurosurgical Institute and 2Department of Neurosurgery, Beijing Tiantan Hospital, Capital Medical University, Beijing, China

Object. Whether selective amygdalohippocampectomy (SelAH) has similar seizure outcomes and better neuropsychological outcomes compared with anterior temporal lobectomy (ATL) is a matter of debate. The aim of this study was to compare the 2 types of surgery with respect to seizure outcomes and changes in IQ scores.

Methods. PubMed, Embase, and the Cochrane Library were searched for relevant studies published between January 1990 and September 2012. Studies comparing SelAH and ATL with respect to seizure and intelligence outcomes were included. Two reviewers assessed the quality of the included studies and independently extracted the data. Odds ratios and standardized mean deviations with 95% confidence intervals were used to compare pooled proportions of freedom from seizures and changes in IQ scores between the SelAH and ATL groups.

Results. Three prospective and 10 retrospective studies were identified involving 745 and 766 patients who underwent SelAH and ATL, respectively. The meta-analysis demonstrated a statistically significant reduction in the odds of seizure freedom for patients who underwent SelAH compared with those who underwent ATL (OR 0.65 [95% CI 0.51–0.82], p = 0.0005). The differences between the changes in all IQ scores after the 2 types of surgery were not statistically significant, regardless of the side of resection.

Conclusions. Selective amygdalohippocampectomy statistically reduced the odds of being seizure free compared with ATL, but the clinical significance of this reduction needs to be further validated by well-designed randomized trials. Selective amygdalohippocampectomy did not have better outcomes than ATL with respect to intelligence.

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Key Words • temporal lobe epilepsy • anterior temporal lobectomy • selective amygdalohippocampectomy • meta-analysis

Abbreviations used in this paper: ATL = anterior temporal lobectomy; FCD = focal cortical dysplasia; FIQ = full-scale IQ; HS = hippocampal sclerosis; MTLE = mesial temporal lobe epilepsy; NTLE = neocortical temporal lobe epilepsy; PIQ = performance IQ; SelAH = selective amygdalohippocampectomy; SMD = standardized mean deviation; VIQ = verbal IQ.

Mesial temporal lobe epilepsy (MTLE) due to hippocampal sclerosis (HS) is the most common drug-resistant disorder observed in epilepsy surgery programs, accounting for 17%–31% of surgical procedures for epilepsy.27 Surgery has been proven to be an effective treatment modality for patients with MTLE, with postoperative seizure-free rates ranging from 59% to 89%.20 Falconer and Taylor introduced standardized anterior temporal lobectomy (ATL) for MTLE in 1968,8 and the procedure has been frequently used for many years. This method removes 4–6 cm of the anterior temporal lobe, including the amygdala and hippocampus. Some depth electrode studies revealed that seizures usually originate from these abnormal mesial structures,4,10 suggesting that resection of the mesial structures alone may be sufficient for obtaining seizure control. Selective amygdalohippocampectomy (SelAH), a procedure developed by Niemeyer in 1958,25 produces postoperative seizure outcomes that are comparable to those attained after ATL.26,30 Moreover, some studies have indicated that SelAH has better neuropsychological outcomes6,14 and a lower risk of visual field defects22 than ATL. On the other hand, some investigators have recorded neocortical epileptiform spikes with cortical electrodes1,35 indicating that tailored resection of the temporal neocortex is
essential for MTLE. Other studies have suggested that better seizure outcomes were achieved in patients who underwent ATL than in those who underwent SelAH, and that no significant differences in neuropsychological outcomes were found between the surgical strategies.

A review attempted to pool studies comparing ATL and SelAH for MTLE to test the hypothesis that the latter procedure produces similar seizure and favorable neuropsychological outcomes, and the conclusion was concordant with the hypothesis. However, no meta-analysis of outcome differences between the surgical strategies has been performed. Since the studies comparing the procedures have conflicting results, a meta-analysis of prior studies could help define the optimal treatment. The aim of the present systematic review and meta-analysis was to determine if SelAH is the superior approach and whether this method might lead to similar seizure and better neuropsychological outcomes than ATL for patients with MTLE.

Methods

Search Strategy

A comprehensive literature search of PubMed, Embase, and the Cochrane Library was conducted by 2 of the authors using the following terms alone or in combination: temporal lobe epilepsy, mesial temporal sclerosis, mesial temporal lobe epilepsy, hippocampal sclerosis, amygdalohippocampectomy, and amygdalo-hippocampectomy. We also searched bibliographies of reviews and book chapters and consulted experts on epilepsy surgery about other studies. Searches were restricted to English-language articles published from 1990 to 2012.

Study Selection, Data Gathering, and Quality Assessment

Two authors independently reviewed the abstract or full text of retrieved manuscripts and applied the following study inclusion criteria: for seizure outcome analyses, 1) articles comparing seizure outcomes in patients after SelAH or ATL, 2) studies with a mean or median follow-up of 1 year or longer, and 3) the use of Engel classification or other comparable schemes to measure postoperative seizure outcome; and for neuropsychological analysis, 1) articles comparing IQ scores measured using the Wechsler Adult Intelligence Scale-Revised in patients who underwent SelAH or ATL, 2) the mean and standard deviation of IQ score could be derived from the paper, and 3) a clear definition of the side of language dominance in all patients. We excluded studies with any overlapping patient populations from the same center. The most recent or complete article was used when the same population was included in multiple articles.

The following data were extracted: the first author’s name; year of publication; country and institution of investigation; sample size; duration of follow-up; seizure-free rate; and mean value and standard deviation of the VIQ, PIQ, and FIQ before and after surgery. When possible, the outcome data were gathered according to the last follow-up. Two authors independently extracted all data, and discrepancies were resolved through discussion.

All studies were rated on the level of evidence using the scheme of evidence classification developed by the Centre for Evidence-Based Medicine in Oxford, United Kingdom. Because no randomized trial was included in our analysis, the methodological quality of these studies was evaluated using the modified Newcastle-Ottawa Scale. This scale uses a star rating system to assess 3 categories, including patient selection, comparability of the study groups, and assessment of the outcome; studies that achieved 6 or more stars were considered to be of high quality.

Data Synthesis and Analysis

Changes in VIQ, PIQ, and FIQ scores were reported as differences between arithmetic means before and after surgery. The standard deviations of these differences were estimated using the following equation:

$$SD_{difference} = \sqrt{SD_{preop}^2 + SD_{postop}^2 - 2 \times Corr \times SD_{preop} \times SD_{postop}}$$

As suggested by Follmann et al., we used an imputed correlation coefficient (Corr) of 0.5 between preoperative and postoperative values.

Studies were the unit of analysis. Odds ratios with 95% CIs were used to compare pooled proportions of freedom from seizure between the SelAH and ATL groups. Standardized mean deviations with 95% CIs were used to compare pooled values of changes in VIQ, PIQ, and FIQ scores between the SelAH and ATL groups. The heterogeneity of surgical effects across studies was assessed using Q statistics, and I² ≥ 50% was considered substantial heterogeneity. A subgroup analysis was performed to compare seizure control between transcortical and transsylvian SelAH and ATL. A sensitivity analysis was performed to evaluate the stability of the results of our meta-analysis. In this analysis, only studies that scored 6 or more stars were included. Publication bias was assessed visually by using funnel plots. All meta-analyses were performed using Review Manager (version 5.1; Revman; The Cochrane Collaboration) by random or fixed effects model, depending on the presence or absence of heterogeneity. Statistical significance was set at p ≤ 0.05.

Results

Evidence Base

The initial database and hand search yielded 345 records. After duplication screening, we identified 194 potentially eligible papers, of which 36 papers remained after the title and abstract review. Thirty-one articles that included 1511 cases (745 cases underwent SelAH and 766 cases underwent ATL) fulfilled the predefined inclusion criteria and were included in the final analysis after full-text review (Fig. 1).

Among the 13 articles, 9 articles were included in seizure and intelligence outcome analyses, and 2 articles were included in both. The characteristics of the included stud-
ies are summarized in Table 1. Except for 3 prospective cohort studies (level of evidence: 2b), the other 10 studies were retrospective, among which 3 studies undertook contemporary comparisons (level of evidence: 2b) and 7 studies used historical series as a control (level of evidence: 4).

Overall, the quality of the included studies was generally low. No randomized trial was identified in the present meta-analysis. Among the 3 prospective studies, only 1 study developed an appropriate protocol to compare SelAH and ATL in the treatment of TLE, which scored 8 stars on the modified Newcastle-Ottawa Scale. The included retrospective studies, especially the studies with nonconsecutive patients, achieved relatively low scores in the Selection and Comparability categories, with the overall scores ranging from 5 to 7 stars. All included studies showed sufficient follow-up for outcome observation, with a minority of participants being lost to follow-up.

**Seizure Outcome**

Eleven studies with 1397 patients with MTLE (686 who underwent SelAH and 711 who underwent ATL) were included in the seizure outcome analysis. Overall, 956 patients (68%) achieved seizure freedom after surgery. The meta-analysis suggested a statistically significant decrease in the odds of seizure freedom for patients who underwent SelAH compared with those who underwent ATL (66% [452 of 686] vs 71% [504 of 711]; OR 0.65 [95% CI 0.51–0.82], p = 0.0005) (Fig. 2 and Table 2). There was no significant heterogeneity among the studies (I² = 43%).
Intelligence Outcome

Four studies met the inclusion criteria for intelligence analysis, in which all the participants were adults and were right handed or had left hemisphere language dominance. Regarding right-side surgery, the majority of patients had an improvement in IQ score after surgery regardless of the surgical strategy. Although the changes in VIQ, PIQ, and FIQ scores tended to be higher in patients who underwent ATL than in those who underwent SelAH, the differences in the changes did not reach statistical significance (VIQ: SMD -0.09 [95% CI -0.36 to 0.19], p = 0.53; PIQ: SMD -0.20 [95% CI -0.48 to 0.08], p = 0.16; FIQ: SMD -0.18 [95% CI -0.46 to 0.09], p = 0.19) (Fig. 3 and Table 2). No significant heterogeneity between the studies was observed in the 3 analyses. In the left-side resections, most of the IQ scores, except the VIQ scores, improved after both types of surgery. Similar to right-side surgery, the differences in the changes for all the types of IQ scores after the 2 types of surgery were not statistically significant (VIQ: SMD -0.24 [95% CI -0.52 to 0.04], p = 0.09; PIQ: SMD -0.21 [95% CI -0.48 to 0.07], p = 0.14; FIQ: SMD -0.19 [95% CI -0.46 to 0.08], p = 0.17) (Fig. 4 and Table 2), with no significant heterogeneity among different studies.

Subgroup Analysis

The subgroup analysis suggested that patients in the transcortical and transsylvian SelAH groups had lower odds of being seizure free than those in the ATL groups (transcortical SelAH vs ATL: 67% [229 of 341] vs 73% [280 of 386], OR 0.68 [95% CI 0.49–0.96], p = 0.03; transsylvian SelAH vs ATL: 65% [211 of 323] vs 71% [185 of 261], OR 0.60 [95% CI 0.41–0.87], p = 0.007) (Fig. 2). A subgroup analysis was not performed for changes in IQ scores because the data were insufficient.

Sensitivity Analysis and Publication Bias

In the sensitivity analysis for seizure outcomes, 3 low-quality studies that scored fewer than 6 stars were excluded, and 8 studies that scored 6 or more stars were included. The sensitivity analysis demonstrated that the significance of seizure outcome was not altered with the exclusion of low-quality studies (OR 0.57 [95% CI 0.43–0.76], p = 0.0001).

Figure 5 shows a funnel plot of the studies included in the meta-analysis for seizure outcomes. All studies were located inside the 95% CI except the study by Mackenzie et al.,21 with a roughly symmetrical distribution around the OR (vertical line), indicating a mild publication bias.

Discussion

The main finding of this meta-analysis was that ATL had a higher odds of controlling seizures than SelAH for patients with MTLE, and the 2 types of surgery showed comparable effects on intelligence. Since the quality of the included studies in our meta-analysis was generally low and the difference of seizure-free rates (66% vs 71%) in the 2 groups was relatively small, the clinical significance of our finding requires further study.

Among the 11 studies included for seizure outcome analysis, 7 studies indicated similar postoperative seizure outcomes in patients who underwent SelAH and ATL.7,23,26,30,31,37,39 However, the statistical result changed to favor ATL when data were pooled from various stud-
ies. The main difference between SelAH and ATL with respect to surgical technique is the resection of the anterolateral temporal neocortex. Thus, the difference in seizure control between the 2 types of surgery is likely associated with the anterolateral temporal neocortex. A pathological study by Piao et al. demonstrated that among a series of 73 patients identified as having HS, dual pathology, including temporal FCD, scar lesions, or tumors were observed in 70 patients. Focal cortical dysplasia was the most common lesion accompanying HS, and 75.5% of cases of FCD were Type 1b.29 Although dual pathology was not frequently identified in other studies, its occurrence ranged from 15% to 30%.20,32 Some extramesiotemporal lesions such as cortical scars, tumors, and vascular malformations were recognized on MRI; however, not all FCD variants could be reliably detected by high-resolution MRI.24 Thus, MTLE patients with another MRI-negative lesion outside the mesial temporal structures might achieve poor seizure outcomes after SelAH.

Some neuroimaging and neuroelectrophysiological studies focusing on the functions of the temporal pole in mesial temporal lobe seizures could also explain the sta-

**Table 2: Comparison of seizure and intelligence outcomes between SelAH and ATL**

<table>
<thead>
<tr>
<th>Outcomes of Interest</th>
<th>No. of Studies</th>
<th>SelAH</th>
<th>ATL</th>
<th>OR/SMD (95% CI)</th>
<th>p Value</th>
<th>Study Heterogeneity</th>
<th>I²</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>seizure outcome</td>
<td>11</td>
<td>686</td>
<td>711</td>
<td>OR 0.65 (0.51 to 0.82)</td>
<td>0.0005</td>
<td>43%</td>
<td>0.06</td>
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<tr>
<td>VIQ, rt resection</td>
<td>4</td>
<td>106</td>
<td>98</td>
<td>SMD -0.09 (-0.36 to 0.19)</td>
<td>0.53</td>
<td>0%</td>
<td>0.98</td>
<td></td>
</tr>
<tr>
<td>PIQ, rt resection</td>
<td>4</td>
<td>106</td>
<td>98</td>
<td>SMD -0.20 (-0.48 to 0.08)</td>
<td>0.16</td>
<td>0%</td>
<td>0.99</td>
<td></td>
</tr>
<tr>
<td>FIQ, rt resection</td>
<td>4</td>
<td>106</td>
<td>98</td>
<td>SMD -0.18 (-0.46 to 0.09)</td>
<td>0.19</td>
<td>0%</td>
<td>0.94</td>
<td></td>
</tr>
<tr>
<td>VIQ, lt resection</td>
<td>4</td>
<td>118</td>
<td>97</td>
<td>SMD -0.24 (-0.52 to 0.04)</td>
<td>0.09</td>
<td>47%</td>
<td>0.13</td>
<td></td>
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<tr>
<td>PIQ, lt resection</td>
<td>4</td>
<td>118</td>
<td>97</td>
<td>SMD -0.21 (-0.48 to 0.07)</td>
<td>0.14</td>
<td>0%</td>
<td>0.94</td>
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<td>4</td>
<td>118</td>
<td>97</td>
<td>SMD -0.19 (-0.46 to 0.08)</td>
<td>0.17</td>
<td>0%</td>
<td>0.66</td>
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</tr>
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Fig. 2. Forest plot and meta-analysis of postoperative seizure-free rates. M-H = Mantel-Haenszel.
Fountas et al. detected altered ipsilateral temporal pole metabolism in patients with HS by using proton MR spectroscopy, and these metabolic changes were associated with permanent histological abnormalities. Chabardès et al. used stereotactic electrodes to record the activities of the temporal polar cortex and mesiotemporal structures in patients with MTLE. In 48% of patients, the temporal pole was involved at the onset of the seizure, before or concurrently with the hippocampus. Therefore, the authors postulated that this phenomenon could be a supplementary explanation for some failures of SelAH.

For patients with MTLE, neuropsychological assessments are routine in some comprehensive epilepsy centers. Several studies compared the 2 surgical procedures with respect to outcomes in memory and language. Some authors have found that preoperative IQ was a predictor of postoperative seizure outcomes in patients with MTLE, with the result suggesting that patients with lower preoperative FIQ scores tended to have recurrent seizures. The 4 studies included for intelligence analysis demonstrated that most IQ scores improved, except VIQ scores, after left-side resection. The pooled data indicated that the changes in IQ scores did not differ significantly between the SelAH and ATL groups regardless of the surgical procedure or the side of resection. Thus, additional resection of the temporal pole might not affect the improvement of IQ scores in patients with MTLE.

The present meta-analysis has several limitations that should be noted. First, the main limitation is the low quality of the included studies, among which there were 3 nonrandomized prospective studies and 10 retrospective studies. The risk of bias may have increased due to inadequate random sequence generation and a lack of blinding. Second, as Schramm mentioned, the distinction between MTLE and neocortical temporal lobe epilepsy was not often made in older papers, which might lead to a result favoring ATL. Although only 3 relatively older studies were included in the present meta-analysis, this limitation should be taken into account. Finally, previous studies discussed memory decline after SelAH or ATL; it is necessary to analyze the differences between the 2 procedures with respect to postoperative memory decline. However, different memory tests were used in the yielded studies, and it was therefore difficult to pool the continuous data due to the variability of tests.

Future research should include well-designed randomized trials with sufficient sample sizes to compare SelAH and ATL regarding seizure outcome, IQ scores, memory, language ability, visual deficits, and other complications or adverse effects. Preoperative evaluation is critical to avoid bias; in addition, the analysis of ictal se-
Meta-analysis of SelAH versus ATL

A

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>SelAH</th>
<th>ATL</th>
<th>Std. Mean Difference</th>
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<td></td>
<td>Mean</td>
<td>SD</td>
<td>Total</td>
</tr>
<tr>
<td>Goldstein 1993</td>
<td>-1.72</td>
<td>11.4</td>
<td>14</td>
</tr>
<tr>
<td>Morino 2006</td>
<td>5.8</td>
<td>12.1</td>
<td>18</td>
</tr>
<tr>
<td>Tanriverdi 2007</td>
<td>3.4</td>
<td>11.6</td>
<td>14</td>
</tr>
<tr>
<td>Tanriverdi 2010</td>
<td>-1.14</td>
<td>14.6</td>
<td>72</td>
</tr>
<tr>
<td>Total (95% CI)</td>
<td>118</td>
<td>97</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

Heterogeneity: Chi² = 5.69, df = 3 (P = 0.13); I² = 47%
Test for overall effect: Z = 1.71 (P = 0.09)

B

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>SelAH</th>
<th>ATL</th>
<th>Std. Mean Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Total</td>
</tr>
<tr>
<td>Goldstein 1993</td>
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<td>18.5</td>
<td>14</td>
</tr>
<tr>
<td>Morino 2006</td>
<td>7.7</td>
<td>17</td>
<td>18</td>
</tr>
<tr>
<td>Tanriverdi 2007</td>
<td>1.1</td>
<td>15.7</td>
<td>14</td>
</tr>
<tr>
<td>Tanriverdi 2010</td>
<td>2.9</td>
<td>12.3</td>
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<tr>
<td>Total (95% CI)</td>
<td>118</td>
<td>97</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

Heterogeneity: Chi² = 0.40, df = 3 (P = 0.94); I² = 0%
Test for overall effect: Z = 1.49 (P = 0.14)

C

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>SelAH</th>
<th>ATL</th>
<th>Std. Mean Difference</th>
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<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Total</td>
</tr>
<tr>
<td>Goldstein 1993</td>
<td>-0.93</td>
<td>10.2</td>
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<td>Morino 2006</td>
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<tr>
<td>Tanriverdi 2007</td>
<td>3.8</td>
<td>12.6</td>
<td>14</td>
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<td>0.6</td>
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<td>72</td>
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<tr>
<td>Total (95% CI)</td>
<td>118</td>
<td>97</td>
<td>100.0%</td>
</tr>
</tbody>
</table>

Heterogeneity: Chi² = 1.59, df = 3 (P = 0.66); I² = 0%
Test for overall effect: Z = 1.36 (P = 0.17)

Fig. 4. Forest plot and meta-analysis of changes in VIQ (A), PIQ (B), and FIQ (C) scores after left resection.

Fig. 5. Funnel plots illustrating the meta-analysis of postoperative seizure-free rates. SE = standard error.
miology, high-resolution MRI with dedicated sequences, and intracranial electroencephalography are useful to identify NTLE and dual pathology in surgical candidates.

**Conclusions**

This study suggests that SelAH is associated with a statistically significant reduction in the odds of being seizure free in patients with MTLE. Moreover, SelAH is not advantageous over ATL with respect to the effects on intelligence. Future large-sample, well-designed, and randomized trials are needed to confirm and update our findings.

**Acknowledgment**

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**Disclosure**

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**References**

27. Pasquier B, Pécot’s M, Fábreg-Bocquentin B, Bensaïda L, Pas-
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