Psychiatric outcomes after temporal lobe surgery in patients with temporal lobe epilepsy and comorbid psychiatric illness: A systematic review and meta-analysis

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ABSTRACT

Background: The currently available evidence is unclear in regard to psychiatric outcomes of temporal lobe epilepsy (TLE) in patients with comorbid psychiatric disorders (PD).

Aim: To identify and synthesize psychiatric outcomes in patients with TLE and comorbid psychiatric illnesses before and after TLE surgery.

Methods: Studies were included if participants were adults and/or children with temporal epilepsy and comorbid psychiatric illness. Surgical interventions included focal resection (e.g., lobectomy, selective amygdalohippocampectomy) or stereotactic laser ablation. Included studies reported on pre- and post- surgery data of comorbid psychiatric illness (e.g., mood and anxiety disorders, depression, psychosis, adjustment disorders, non-epileptic seizures, and personality disorders).

Results: Ten studies were included in the review. The proportion of patients achieving PD resolution or improvements after surgery varied widely between studies, ranging from 15 % to 57 % at the reported follow-up time. Three studies reported on PD symptom worsening after surgery, with considerable variations of patient proportions across studies. Meta-analysis suggests that 43 % of patients demonstrated improvement and 33 % of patients showed a worsening in psychiatric scores across all studies. Preliminary data from three studies suggest that seizure control may be associated with favourable psychiatric outcomes.

Conclusion: A considerable proportion of reported TLE patients with comorbid psychiatric illnesses have improvement in their psychiatric symptoms after temporal lobe epilepsy surgery. There is scarcity of detailed outcome reporting including symptom scores, and to date, predictive factors for favourable vs unfavourable outcomes in this patient population are not clear. Further research on the topic is warranted.

1. Introduction

Surgery for refractory temporal lobe epilepsy (TLE) is an effective treatment modality and is reported to have roughly a 60–70% chance of seizure freedom at a 2-year follow-up (Engel, 1996). Patients with epilepsy have a higher prevalence of lifetime psychiatric disorders (35%) compared to the general population (21 %), with mood and anxiety disorders being the most frequent psychiatric comorbidities in patients with epilepsy, compared to the general population (Tellez-Zenteno et al., 2007). Psychiatric comorbidities may be an independent predictor of seizure outcomes, with worse seizure-freedom prognosis reported post-surgery in the presence of psychiatric disorders (Kanner et al., 2009).

For many TLE patients, the long-term psychosocial benefits after
surgery are significantly more favourable compared to patients who are treated with medication (Jones et al., 2002; Mikati et al., 2006). However, following TLE surgery, psychiatric symptoms can develop de novo or pre-existing symptoms may worsen, which can impair an otherwise good surgical outcome and result in significant distress for patients (Moss et al., 2009).

In comparison to an emphasis on neuropsychological and neurological sequelae of TLE surgery, studies examining psychiatric complications following TLE surgery are limited and usually focus on pre- and post-operative psychopathology and risk factors for poor psychiatric outcome. Two previous systematic reviews on the topic of psychiatric outcomes after TLE surgery were identified: Macrodimitris et al. (2011) found 13 studies, demonstrating either improvements in psychiatric outcome post-surgery or no changes in psychiatric outcome. The two main predictors of psychiatric outcomes were freedom from seizure activity, and presurgical psychiatric history, with some studies showing that de novo psychiatric issues occurred primarily in patients with continued seizures after surgery, and that surgical patients with a history of psychiatric issues are more likely to experience psychiatric problems postsurgery (Macrodimitris et al., 2011). The systematic review by Cleary et al. (2013) identified 39 studies on the topic of psychiatric comorbidities after TLE surgery. The authors found inconsistent findings in the studies comparing depression before and after temporal lobe surgery, with a number of studies showing improvements in depression after surgery, defined either as a reduction in the number of patients meeting the clinical criteria for depression, or significant improvements in rating scales measuring depressive symptomatology (Cleary et al., 2013). Significant gains in seizure control were related to improvements in depression after surgery, however, these findings were not consistent. With regard to anxiety, the majority of studies showed a reduced prevalence of anxiety postoperatively, but results were inconsistent. Predictors of post-surgical anxiety was a previous history of anxiety or depression before surgery. The authors of this review concluded that despite the available evidence, it is not known whether different pre-operative neuropsychological phenotypes are more at risk of poor post-surgical psychiatric outcome (Cleary et al., 2013).

With discrepancies in results and no recent systematic review on the topic identified, the aim of the current systematic review was to identify and synthesize the evidence of psychiatric outcomes in patients with TLE and comorbid psychiatric illnesses before and after TLE surgery.

2. Methods

2.1. Search strategy

A systematic database literature search was performed from Database start up until May 2021, using the following databases: Embase (via Embase.com), Medline (via PubMed), and the Cochrane Library. Additional references were identified by handsearching bibliographies of included studies. For the identification of grey literature, such as dissertations or reports, google scholar was searched.

The search strategy included keywords relating to the inclusion criteria, i.e. temporal lobe epilepsy, temporal lobe resection, psychiatric disorders, anxiety, depression. The detailed Medline search strategy, which was adapted to the other databases, is provided as a supplement.

2.2. Eligibility criteria

The inclusion criteria were adults and children with temporal epilepsy and comorbid psychiatric illness. The studies were limited to English language studies, prospective or retrospective controlled/ uncontrolled or randomized controlled trials (RCTs). Surgical interventions included focal resection (e.g. lobectomy, selective amygdalohippocampectomy) or stereotactic laser ablation. Included studies reported on pre- and postsurgery data of comorbid psychiatric illness (e.g., mood and anxiety disorders, depression, psychosis, adjustment disorders, non-epileptic seizures, and personality disorders). Diagnoses of psychiatric disorders in the included literature were made using the Diagnostic and Statistical Manual of Mental Disorders (DSM; American Psychiatric Association, 2000) criteria or International Classification of Diseases (ICD; World Health Organization, 1992) criteria for psychiatric diagnoses or used a clear psychometrically sound self-report symptom scale; and used a systematic method for obtaining information (e.g., review by psychiatrist, structured clinical interview, rating scales).

Studies in any other language than English were excluded. Studies which reported data from patients with and without PD together without stratification for these patient populations, were excluded.

2.3. Study selection and data extraction

The first selection step included the scanning of the references obtained from the database searches by two reviewers based on titles and abstracts and the pre-specified selection criteria. Any discrepancies were reconciled by discussion. A more detailed screening was carried out based on the full-text articles of the previously included papers against the eligibility criteria, and any uncertainties were reconciled by discussion. The data extraction was performed by two reviewers by populating data from the included studies into a pre-designed data extraction table, including general study data as well as information on study outcomes. Of particular interest were predictive factors with regard to postsurgical psychiatric outcomes, such as right vs. left resection, age of patients, degree of epilepsy (as measured by Engel and International League against epilepsy [ILAE] scales), type and severity of psychiatric comorbidity, type of surgical intervention (open temporal lobe resection vs stereotactic laser ablation). Any disagreements between the reviewers were resolved by discussion. When necessary, the authors of the original publications were contacted for additional information.

2.4. Statistical analysis

The proportion of patients with reported improvement in psychiatric scores as well as worsening of psychiatric scores were separately analyzed using the metaprop routine of the meta package version 5.1–1 of the statistical software R (version 4.1.2). Resultant forest plots stratified by group were obtained.

The critical appraisal utilized the appropriate checklist provided by the Joanna Briggs Institute (JBI, 2021).

The reporting of this present systematic review is based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

3. Results

3.1. Study searches and selection

The systematic database search yielded a total of 3335 records. After removal of duplicates and excluding studies as per eligibility criteria, 64 full-text articles were assessed for inclusion in this review. After exclusion of 54 articles, 10 final studies were included in this review (Fig. 1).

3.2. Study characteristics

Of the 10 included studies, two were prospective case series and the remaining 8 studies were experimental studies with pre- and post-test design. Only three studies were identified that were conducted in the last 10 years. The number of participants varied greatly between studies, from 22 (Cankurtaran et al., 2005) to 115 (De Araujo-Filho et al., 2012) in the experimental studies to 14 in the two case series. A total number of 496 patients participated in the identified experimental studies. Eight studies included only adults, with an age range of 18–65 years, one study included adults and children, and one study included children only (McLellan et al., 2005).
In terms of method of resection, eight studies reported temporal lobectomy as surgical method, in one study a cortico-amygdalo-hippocampectomy was performed (De Araujo-Filho et al., 2012) and one study did not report on this method (Pintor et al., 2007).

The most common PDs assessed were anxiety and depression, and the assessment tools were validated. These outcomes were assessed mainly through structured clinical interview and/or self-report measures.

The follow-up periods varied considerably between studies, ranging from one month to 30 years, with most studies reporting rather short follow-up times (up to 2 years) and only four studies having longer follow-up times (5 years and beyond) (Benevides et al., 2021; de Araujo-Filho et al., 2012; Stevens et al., 1990; Jensen et al., 1979).

A total of seven studies reported results stratified by the PD, and in three studies the results after surgery were not stratified by PD, i.e. generally reported for all patients suffering from PD at a given timepoint.

### 3.3. Study results

Across the 10 included studies, all reported on the pre- and postsurgical number of patients with PD only; no mean PD-scores of these cohorts were reported. Only three studies conducted an analysis with regard to the degree of epilepsy as a predictive factor for postsurgical psychiatric outcomes in patients with presurgical PD (D’Alessio et al., 2014; De Araujo-Filho et al., 2012; Jensen et al., 1979); all other studies did not consider these factors in their analysis.

In those studies with results stratified by PD, a resolution of PD was achieved in a substantial proportion of patients. In those with psychosis (D’Alessio et al., 2014), the proportion of patients in whom the psychosis had resolved was 43%. In patients with anxiety and depression, these numbers varied considerably, ranging from 23% (Derry et al., 2000) to 83% (Cankurtaran et al., 2005) with PD resolution. In patients with other PD, only one study reported on the proportion of patients with resolution of symptoms, which was 21% in children. Improvements of PD symptoms also varied substantially, ranging from 19% in patients with depression (Derry et al., 2000) to 40% in patients with other PD (Jensen et al., 1979) (Table 1).

These results are reflected in the studies without stratification of results by PD, with the proportion of PD resolution ranging widely from 15% (Glosser et al., 2000) to 57%, which was also the study with the largest sample size and cortico-amygdalo-hippocampectomy as surgical method (De Araujo-Filho et al., 2012). These studies did not report data on improvements of PD (Table 2).

Across all studies, only three reported on worsening of symptoms, with 19% in patients with depression (Derry et al., 2000), 21% in patients with psychosis (D’Alessio et al., 2014) and between 7% and 36% in children with other PD (McLellan et al., 2005) (Table 1).

There appears to be no marked difference between the numbers of resolved/improved cases after surgery in those studies that had longer follow-up times (5 years and beyond) compared to those with shorter follow-up times (up to 2 years). Three studies reported on the impact of
Table 1: Studies with results stratified by PD.

| Study                        | Study subjects (N) | Age group                      | Study type   | Method of resection | Psychiatric variables (Assessment tool) | Follow-up | Results                                                                 |
|------------------------------|--------------------|--------------------------------|--------------|---------------------|----------------------------------------|-----------|------------------------------------------------------------------------|
| **Psychosis**                |                    |                                |              |                     |                                        |           |                                                                         |
| D’Alessio et al. (2014)¹¹    | 14                 | Adults (mean age 27.4 years, range 20-65 years) | Case series  | Temporal lobectomy  | Psychosis (GAF7)                       | 1 year, 2 years | All 14 patients were diagnosed with psychosis before surgery. At 2 years FU after surgery: No psychosis: n = 6 out of 14 (43%) No change: n = 3 out of 14 (21%) Worsened: n = 3 out of 14 (21%); developed acute and transient psychotic symptoms De novo: n = 2 out of 14 (14%); depression Total GAF scores were significantly higher after surgery (p < 0.05) in the total patient population (GAF scores not available). Total GAF scores were significantly higher after surgery (p < 0.05) in patients found to be in Engel class I-II (GAF scores not available). |
| **Depression/Anxiety**       |                    |                                |              |                     |                                        |           |                                                                         |
| Benevides et al. (2021)¹²    | 44                 | Adults (Mean age 34.3 years)    | Pretest-Posttest | Temporal lobectomy  | Anxiety and depression (HADS)          | 1.36 months and yearly after that for at least 4 years; mean 104 months (range 70–130) | Before surgery n = 19 patients (43%) had depression and/or anxiety At the last follow-up after surgery: No PD: n = 9 out of 19 (47%) Had anxiety and/or depression: n = 10 out of 19 (53%) |
| Derry et al. (2000)¹⁴        | 39                 | Adults (mean age 31.2 years, range 18–51) | Pretest-Posttest | Temporal lobectomy  | Depression (CES-D)                     | 2 years   | Before surgery n = 16 patients (41%) had depression At 2 years after surgery: No depression: n = 9 out of 16 (23%) No change: n = 1 (6%) Improvements: n = 3 out of 16 (19%) Worsening: n = 3 out of 16 (19%) |
| **Other PD**                 |                    |                                |              |                     |                                        |           |                                                                         |
| McElhan et al. (2005)¹⁵      | 60                 | Children (mean age 10 y 7mo, range 7mo – 17 y 11mo) | Pretest-Posttest | Temporal lobectomy  | One or more DSM-IV psychiatric diagnosis (pre-post assessment) | 1 year | Before surgery n = 43 patients (72%) had PD At 1 year after surgery: No PD: n = 9 out of 43 (21%) No change: n = 7 out 23 (30%) with PDD, n = 5 out of 14 (36%) with ADHD, n = 4 out of 14 (29%) with ODD/CD, n = 8 out of 25 (32%) with DBD, n = 1 out of 5 (20%) with emotional disorder Improvements: n = 11 out 23 (48%) with PDD, n = 5 out of 14 (36%) with ADHD, n = 2 out of 14 (14%) with ODD/CD, n = 8 out of 25 (32%) with DBD Worsened: n = 3 out 23 (13%) with PDD, n = 1 out of 14 (7%) with ADHD, n = 5 out of 14 (36%) with ODD/CD, n = 4 out of 25 (16%) with DBD, n = 1 out of 5 (20%) with emotional disorder, n = 1 out of 1 (0%) with eating disorder |
| Stevens et al. (1990)¹⁶      | 14                 | Adults (age range 20-47 years)  | Case series  | Temporal lobectomy  | Paranoia, suspicion, irritability (not reported) | 20-30 years | Before surgery n = 5 patients (36%) had PD (n = 3 paranoid personality, n = 1 suspicion, n = 1 severe irritability) At 20-30 years after surgery: No change: n = 3 out of 5 (60%); n = 2 patients with paranoid personality and n = 1 with suspicion had a paranoid psychosis Improvements: n = 2 out of 5 (40%); n = 1 with severe irritability, n = 1 with paranoid personality |
| Jensen et al. (1979)²⁷       | 74                 | Adults, children (age range 4-54 years) | Pretest-Posttest | Temporal lobectomy  | Behaviour, psychosis, neurosis, sexual aggression, suicidal tendencies (not reported) | 10 years | Before surgery n = 63 patients (85%) had PD At 10 years after surgery: Improvements or no PD: n = 33 out 54 (61%) with behaviour disturbance, n = 6 out 11 (55%) with psychosis, n = 9 out 11 (82%) with suicidal attempts, n = 5 out 7 (71%) with neurosis, n = 1 out 4 (25%) with sexual aggression The remaining patients remained unchanged or deteriorated. (continued on next page) |
the degree of epilepsy on psychiatric outcomes, with patients classified as Engel I/II in terms of seizure control achieving more favourable outcomes compared to those with Engel III classification (D’Alessio et al., 2014, de Araujo-Filho et al., 2012, Jensen et al., 1979).

In none of the studies, the severity of pre- and postsurgical PD was reported.

The study characteristics and results of the included trials are summarized in Table 1 and Table 2.

Approximately 43% of patients demonstrated improvement in psychiatric scores across all studies (Fig. 2). The overall random effects model suggests that 43% of the population undergoing lobectomy had their psychiatric symptoms improved. There does not appear to be a robust difference among the four study sub-populations.

Approximately 33% of patients demonstrated a worsening of psychiatric symptoms (Fig. 3). Slight differences among different psychiatric disease categories were noted.

4. Discussion

The aim of the present systematic review was to identify and synthesize the evidence of psychiatric outcomes in patients with TLE and comorbid psychiatric illnesses before and after TLE surgery. The results of this systematic review indicate that the proportion of patients achieving PD resolution or improvements after surgery varied widely between studies, ranging from 15% to 57% at the reported FU-time, with a combined improvement across all studies of 43%. Only three studies reported on PD symptom worsening after surgery, with considerable variations of patient proportions across studies, which ranged from 19% in patients with depression and 21% in patients with psychosis to 7% – 36% in children with other PD. The combined proportion of patients with worsening psychiatric symptoms was 33%. Additionally, in the three studies that reported on the impact of the degree of epilepsy on psychiatric outcomes, patients classified as Engel I/II in terms of seizure control achieved more favourable outcomes compared to those with Engel III classification.

### Table 1 (continued)

| Study            | Subjects (N) | Age group | Study type | Method of resection | Psychiatric variables (Assessment tool) | Follow-up | Results |
|------------------|--------------|-----------|------------|---------------------|----------------------------------------|-----------|---------|
| De Araujo-Filho et al. (2012) | 115          | Adults (Mean age 36.0 years) | Pretest-Posttest | Cortico-amygdalo-hippocampectomy | Depression, Anxiety, Psychosis (not reported) | Mean 4.7 years (range 1-8 years) | Before surgery n = 47 patients (41%) had PD (n = 27 depression, n = 11 anxiety, n = 7 psychosis, n = 4 fulfilled criteria for two Axis I disorders) At FU after surgery: No PD: n = 27 out of 47 (57%) The group with only pre-surgical PD contained more patients with Engel II/IC/D (p = 0.002), and the group with pre- and postsurgical PD contained more patients with Engel III (p = 0.04). Before surgery n = 6 patients (27%) had PD (n = 3 social phobia; n = 1 depression; n = 1 bereavement; n = 1 panic disorder) At 3 months after surgery: No PD: n = 5 out of 6 (83%) De novo: n = 1 out of 6 (17%); depression, which resolved at 6 months |
| Cankurtaran et al. (2005) | 22           | Adults (mean age not reported) | Pretest-Posttest | Temporal lobectomy | Anxiety, Depression, Psychiatric disorder (BPRS, HDRS, and HARS) | 3 and 6 months | Improvement in psychiatric status was clearly correlated with relief from seizures (no further data given). |
| Pintor et al. (2007) | 70           | Adults (Mean age 31.1 years) | Pretest-Posttest | Not reported | Anxiety, Depression, Psychiatric disorder (SCID-IV) | 1, 6, and 12 months | Improvement in psychiatric status was clearly correlated with relief from seizures (no further data given). |
| Glosser et al. (2000) | 44           | Adults (mean age 32.2 years) | Pretest-Posttest | Temporal lobectomy | General PD (GAF, BPRS); Anxiety (STAI); Depression (BDI); Mood (POMS) | 6 months | Improvement in psychiatric status was clearly correlated with relief from seizures (no further data given). |

BPRS: Brief Psychiatric Rating Scale; BDI: Beck Depression Index; BAI: Beck Anxiety Index; FU: Follow-up; GAF: Global Assessment of Functionality; HDRS: Hamilton Depression Rating Scale; HARS: Hamilton Anxiety Rating Scale; MDD: Major depressive disorder; ODD/CD: oppositional defiant disorder/conduct disorder; PD: Psychiatric disorder; PDD: Pervasive developmental disorder; POMS: profile of mood states; SCID-IV: Structured clinical interview for DSM-IV Axis I diagnoses; STAI: state-trait anxiety inventory
Makrodimitris et al. (2011) also found in their systematic review that seizure freedom was an important predictor of psychiatric outcomes postsurgery (Makrodimitris et al., 2011). However, Cleary et al. (2013) noted in their systematic review that some of the included studies did not show that seizure freedom robustly predicted post-surgical psychiatric morbidity. They point out that different underlying neurobiological factors and mechanisms may be present depending on time of onset after surgery and type of psychiatric symptoms (Cleary et al., 2013). The improvement of about half of PD-patients after surgery found in the present review sheds more light to the previously held notion of higher likelihood of PD symptoms after surgery if pre-surgical symptoms were present, which was derived from cohort studies comparing psychiatric outcomes of a total cohort and analysing predictive factors. The present results indicate that presurgical PD may not be per se a contraindication for TLE surgery. The specific factors that contribute to the improvement or resolution of psychiatric symptoms, such as seizure improvement or freedom, remain to be determined in future studies.

However, the findings of the present systematic review also highlight that postoperative psychiatric worsening is common (19–21% in adult patients, 7–36% in children), hence, patients should be informed before surgery accordingly. Previous research indicates that as part of the preoperative counselling and informed consent procedure, physicians identified seizure outcome and improvements of quality of life as one of the most significant topics for preoperative discussion, whereas less than 16% addressed psychiatric issues (deMase et al., 2009).

The identified studies were characterized by a considerable heterogeneity due to different methodologies applied, such as the methods of disease classification, PD assessment methods, duration of FU period, sample size and participant characteristics, study design and the effect of treatment. Hence, comparison and arriving at definite conclusions between studies are difficult.

Only three studies were identified that reported on the patient population of interest in the last 10 years, and a total of 10 studies were found, which reflects a general lack of studies on this topic. As previously noted by Cleary et al. (2013) and Makrodimitris et al. (2011), a number of methodological issues were apparent in the included studies. In all identified studies of the present review without exception, only the proportions of patients with comorbid PD before and after surgery were reported on, which is meaningful to establish the success rates of TLE surgery with regard to clearing or improving PD in those affected, however, it does not give an indication about the severity of PD, as no symptom scores were provided, which would make evidence synthesis in form of meta-analysis impossible. Additionally, it currently is unclear what the predicting factors of improvements or worsening in symptoms of PD in the patient population of interest are, as these rarely have been assessed (Makrodimitris et al., 2011; Cleary et al., 2013). Further, most of the symptoms were assessed with self-report questionnaires which may be underreported due to non-disclosure of past or current psychopathology out of fear of surgical disqualification (Kanner et al., 2000; Kanner, 2008; Cleary et al., 2013). With the application of a variety of diagnostic criteria, assessment tools and clinical cut-offs for the assessment of psychiatric status as well as the non-comparability of self-report measures with semi-structured interviews for psychiatric diagnostic procedures (Glosser et al., 2000), a comparison across studies is challenging, as previously pointed out. Since no single method has been identified as being optimal for pre- and post-surgical psychiatric

| Study | Improved | N  | Proportion | 95%-CI |
|-------|----------|----|------------|--------|
| Disease = Psychosis | D’Alessio et al. (2014) | 6  | 0.43 | [0.18; 0.71] |
|       | Random effects model | 14 | 0.43 | [0.21; 0.68] |
|       | Heterogeneity: not applicable | | | |
| Disease = Anxiety/Depression | Benevides et al. (2021) | 9  | 0.47 | [0.24; 0.71] |
|       | Cankurtaran et al. (2005) | 5  | 0.83 | [0.36; 1.00] |
|       | Derry et al. (2000) | 12 | 0.75 | [0.48; 0.93] |
|       | Random effects model | 41 | 0.65 | [0.44; 0.82] |
|       | Heterogeneity: $I^2 = 48\%$, $\tau^2 = 0.1506$, $p = 0.15$ | | | |
| Disease = Other | McLellan et al. (2005) | 9  | 0.16 | [0.07; 0.28] |
|       | Stevens et al. (1990) | 2  | 0.40 | [0.05; 0.85] |
|       | Jensen et al. (1979) | 42 | 0.57 | [0.45; 0.68] |
|       | Random effects model | 136 | 0.35 | [0.15; 0.62] |
|       | Heterogeneity: $I^2 = 90\%$, $\tau^2 = 0.6998$, $p < 0.01$ | | | |
| Disease = Multiple | De Araujo-Filho et al. (2012) | 27 | 0.57 | [0.42; 0.72] |
|       | Pinnor et al. (2007) | 14 | 0.30 | [0.17; 0.45] |
|       | Glosser et al. (2000) | 5  | 0.15 | [0.06; 0.31] |
|       | Random effects model | 133 | 0.33 | [0.16; 0.55] |
|       | Heterogeneity: $I^2 = 87\%$, $\tau^2 = 0.5700$, $p < 0.01$ | | | |

**Fig. 2.** Proportion of patients with improved psychiatric outcome after TLE relative to those who either stayed the same or worsened.
assessments (Guangming et al., 2009), several measures may be the best approach, including a neuropsychiatric evaluation before surgery which may lead to an increase in the predictability of the prognostic models used for neurological outcomes of TLE surgery as well as being able to better inform patients and their families about the psychiatric risks of TLE surgery (Cleary et al., 2013).

Since none of the included studies had a control group, it also is not clear whether surgery per se would be a risk factor for PD in patients with TLE. Psychiatric symptoms may fluctuate over time as a natural course of disease, with or without surgery, hence, worsening or improvements after surgery may well be the result of these fluctuations. Although adding a control group of TLE patients without surgery as part of a study would be desirable from a methodological standpoint, it most likely would pose ethical concerns of withheld treatments. Alternatively, TLE patients who decline surgery for various reasons might be used as control subjects, but the likelihood of recruiting sufficient numbers to compare them to the treatment groups are probably low.

There was also some considerable variety in follow-up times across the identified studies, which may impact interpretability of results. For example, assessing psychiatric status in the months preceding surgery may evoke anxiety and stress which may not represent patients’ usual mood states (Glosser et al., 2000). Additionally, those studies with short FU-times (i.e. up to 2 years) may not detect psychiatric outcomes that may become apparent later on, and vice versa with studies only having long FU-periods (i.e. more than 5 years) potentially missing early psychiatric symptoms (Cleary et al., 2013).

The present systematic review has some limitations, which may influence the results presented: only English language articles were included, which could have excluded relevant articles in other languages. Contacting authors of publications that were published decades ago for further information was not possible as no meaningful contact details were found. Although every effort was undertaken to identify appropriate grey literature on the topic, it might be possible that some relevant research has been missed.

5. Conclusion

The results of this systematic review are the first to show that a considerable proportion (15–57%) of TLE patients with comorbid psychiatric illnesses may benefit from TLE surgery by showing a resolve or improvement in their psychiatric symptoms. Preliminary data suggest that good seizure control may be associated with favourable psychiatric outcomes. However, there is scarcity of detailed outcome reporting including symptom scores as well as data reporting on the proportion of patients that are getting worse, and to date, it is unclear what the predictive factors with regard to improvements, no change, or worsening of PD-symptoms in this patient population are. Therefore, the results of this study have to be interpreted with caution and further research on the topic is warranted before a robust conclusion can be formulated.

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Conflict of interest

The authors have no conflicts of interest to declare.

References

de Araújo Filho, G.M., Mazetto, L., Gomes, F.L., et al., 2012. Pre-surgical predictors for psychiatric disorders following epilepsy surgery in patients with refractory temporal lobe epilepsy and mesial temporal sclerosis. Epilepsy Res. 102 (1–2), 86–93.
Benevides, M.L., Nunes, J.C., Guarnieri, R., et al., 2021. Anxiety and depressive symptoms long after mesial temporal epilepsy surgery: a prospective study. Epilepsy Behav. 118, 107936.
Cankurtaran, E.S., Ulug, B., Saygi, S., et al., 2005. Psychiatric morbidity, quality of life, and disability in mesial temporal lobe epilepsy patients before and after anterior temporal lobectomy. Epilepsy Behav. 7 (1), 116–122.
Cleary, R.A., Baxendale, S.A., Thompson, P.J., et al., 2013. Predicting and preventing psychopathology following temporal lobe epilepsy surgery. Epilepsy Behav. 26 (3), 322–334.
D’Alessio, L., Scévola, L., Lima, M.F., et al., 2014. Psychiatric outcome of epilepsy surgery in patients with psychosis and temporal lobe drug-resistant epilepsy: a prospective case series. Epilepsy Behav. 37, 165–170.
DeMase, D.F., Gruenthal, M., Balint, J., 2009. The national temporal lobectomy survey. Seizure 18 (10), 702–710.
Derry, P.A., Rose, K.J., McLachlan, R.S., 2000. Moderators of the effect of preoperative emotional adjustment on postoperative depression after surgery for temporal lobe epilepsy. Epilepsia 41 (2), 177–185.
Engel, J., 1996. Surgery for seizures. N. Engl. J. Med. 334, 647–652.
Glosser, G., Zwil, A.S., Glosser, D.S., O’Connor, M.J., Sperling, M.R., 2000. Psychiatric aspects of temporal lobe epilepsy before and after anterior temporal lobectomy. J. Neurol., Neurosurg. Psychiatry 68 (1), 53–58.
Guangming, Z., Wenjing, Z., Guoqiang, C., Yan, Z., Fuquan, Z., Huangcong, Z., 2009. Psychiatric symptom changes after corticoamygdalohippocampectomy in patients with medial temporal lobe epilepsy through Symptom Checklist 90 Revised. Surg. Neurol. 72 (6), 587–591.
JBI, 2021. Joanna Briggs Institute. About JBI. Available from URL: https://jbi.global/about-jbi. (accessed 30 May 2021).
Jensen, I.N.G.E., Larsen, J.K., 1979. Mental aspects of temporal lobe epilepsy. Follow-up of 74 patients after resection of a temporal lobe. J. Neurol., Neurosurg. Psychiatry 42 (3), 256–265.
Jones, J.E., Berven, N.L., Ramirez, L., et al., 2002. Long-term psychosocial outcomes of anterior temporal lobectomy. Epilepsia 43 (8), 896–903.
Kanner, A.M., 2008. Should a psychiatric evaluation be included in every pre-surgical work-up?. In: Psychiatric Controversies in Epilepsy, 2008 Elsevier, London, pp. 239–254.
Kanner, A.M., Kozak, A.M., Frey, M., 2000. The use of sertraline in patients with epilepsy: is it safe? Epilepsy Behav. 1 (2), 100–105.
Kanner, A.M., Byrne, R., Chicharro, A., et al., 2009. A lifetime psychiatric history predicts a worse seizure outcome following temporal lobectomy. Neurology 72 (9), 793–799.
Mikati, M.A., Comair, Y.G., Rahi, A., 2006. Normalization of quality of life three years after temporal lobectomy: a controlled study. Epilepsia 47 (5), 928–933.
Moss, K., O’Driscoll, K., Eldridge, P., et al., 2009. Risk factors for early post-operative psychiatric symptoms in patients undergoing epilepsy surgery for temporal lobe epilepsy. Acta Neurol. Scand. 120 (3), 176–181.
Pintor, L., Ballese, E., Fernandez-Egea, E., et al., 2007. Psychiatric disorders in temporal lobe epilepsy patients over the first year after surgical treatment. Seizure 16 (3), 218–225.
Stevens, J.R., 1990. Psychiatric consequences of temporal lobectomy for intractable seizures: a 20–30-year follow-up of 14 cases. Psychol. Med. 20 (3), 529–545.
Tellez-Zenteno, J.F., Patten, S.B., Jetté, N., et al., 2007. Psychiatric comorbidity in epilepsy: a population-based analysis. Epilepsia 48 (12), 2336–2344.