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Review

Predicting and preventing psychopathology following temporal lobe epilepsy surgery

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ABSTRACT

Less than 3% of temporal lobe epilepsy (TLE) surgical outcome studies have investigated the psychiatric sequelae and morbidity associated with surgery. This is disproportionate to the extent of the problem. Variable prevalence rates have been reported for post-surgical depression, anxiety, and interictal psychosis. Until recently, very few studies distinguished de novo postoperative presentations from pre-existing conditions, making it difficult to accurately assess the impact of TLE surgery on psychiatric morbidity. Predictors of de novo postoperative presentations have proved elusive. This current review summarizes the findings from a systematic literature review of the psychiatric morbidity associated with TLE surgery including newly published follow-up data from our own series of 280 surgical patients. A framework for future research, possible pathophysiological mechanisms, and translational models are also discussed.

This article is part of a Special Issue entitled "The Future of Translational Epilepsy Research".

1. Introduction

Neurosurgery for refractory temporal lobe epilepsy (TLE) is an effective treatment, as it carries a 60–70% chance of seizure freedom at 2-year follow-up [1]. For many temporal lobectomy patients, the long-term psychosocial gains are significantly more favorable than for patients who are medically treated [2,3]. Following TLE surgery, however, psychiatric symptoms can develop for the first time (de novo) or pre-existing symptoms may worsen. Accordingly, psychiatric complications may tarnish an otherwise good surgical outcome, resulting in significant distress for patients and their families [4]. Cases of attempted and completed suicide have been reported, paradoxically, in patients who have been rendered seizure free [5,6]. Research data on psychiatric complications following TLE surgery are limited, in sharp contrast to the continuing emphasis on neuropsychological and neurological sequelae [7]. The psychiatric outcome of TLE surgery is of particular interest given the high overall prevalence of psychiatric conditions in persons with TLE ranging from 19 to 80% [8–18], who are now widely considered eligible surgical candidates [19]. Although recognition of psychiatric complications following TLE surgery can be traced back to the 1950s [20,21], it is only in the last 15 years that there has been increased research into this topic [22]. The focus of recent studies has been to clarify preoperative and postoperative psychopathology and, importantly, to identify risk factors for poor psychiatric outcome, thus aiding the surgical decision-making process and enhancing postoperative care.

This current review summarizes the findings from a systematic literature review of the psychiatric morbidity associated with TLE surgery including newly published follow-up data from our own series of 280 surgical patients. We also discuss a framework for future research including possible translational models that may be relevant in investigating the pathophysiological mechanisms.

2. Systematic literature review

A literature search was conducted using Medline, Embase, and PsychINFO until June 2012 with the following search terms: temporal lobe epilepsy, neurosurgical procedures, and mental disorders (e.g., mood and anxiety disorders, psychosis, adjustment disorders, non-epileptic seizures, and personality disorders). Previous literature reviews were excluded [19,23], although reference lists were checked to ensure no additional studies had been missed. The search yielded 4042 articles relating to TLE surgery. Of these, less than 3% (n = 88) reported psychiatric comorbidity as an outcome of surgery. Studies on palliative neurosurgical procedures, stimulation studies, case reports, and studies not published in peer reviewed English language journals were excluded. Thirty-nine studies met these inclusion criteria and, therefore, were included in the review. These studies are summarized in Table 1.

Twenty-four studies were prospective but uncontrolled; eleven were retrospective uncontrolled; three were retrospective controlled and one was prospective controlled. Control groups consisted of patients deemed not eligible for surgery [10], continued on medical

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treatment [24,25], or who did not develop a postoperative mood disorder [26]. The majority of retrospective studies (n = 12) had a follow-up of more than 1 year (range 3 months–30 years). However, one retrospective study did not report their follow-up duration [27]. Unsurprisingly, prospective studies in comparison had a shorter follow-up (2 weeks–8 years).

Depression (twenty-five studies), anxiety (seventeen studies), and interictal psychosis (twelve studies) were the most frequent outcomes explored. These outcomes were assessed mainly through reviewing case-notes, via structured clinical interview and/or self-report measures. Other outcomes received less attention; namely, personality disorders (five studies), postictal psychosis (four studies), non-epileptic seizures (two studies), psychosocial adjustment (one study), behavioral problems (one study), and interictal dysphoric disorder (IDD; one study).

2.1. Depression

The prevalence of preoperative depressive symptoms in TLE patients was highly variable owing to divergent methodologies and diagnostic classifications (range 5–50%) [8,10,28–34].

There are inconsistent findings in the studies comparing depression before and after temporal lobe surgery. A number of studies report improvements in depression after surgery, defined either as a reduction in the number of patients meeting the clinical criteria for depression [8,10,30,33], or significant improvements in rating scales measuring depressive symptomatology [25,31,35].

In contrast, Anhoury and colleagues [36] found no change in prevalence rates of mood disorders pre- and post-surgery. In two studies, it was unclear whether depression prevalence rates had improved or worsened after surgery, as the frequency of patients that developed de novo depression was not reported [30,32].

Although depression improved in some patients in the aforementioned studies, de novo cases of depression (including IDD) were clearly reported in a minority of cases [8,10,25,28,29,31,34–39].

In studies that only included temporal lobectomy patients, de novo depression prevalence rates ranged from 4% [25] to 18% [28]. Findings shown in Table 1 suggest that de novo depression frequently occurs within 3–12 months after surgery [10,28] and tends to persist (range 1–11 months) [8]. However, determining the evolution of depression is challenging, owing to the varied and limited time-frames in which psychiatric function is assessed.

Regarding predictors of post-surgical depression, ten studies demonstrated that improvements in depression after surgery were related to significant gains in seizure control [10,25,31,32,35,37-40]; however, this was not a consistent finding [8,34,42,44,72].

There is little evidence to suggest that post-surgical depression is associated with the laterality of the surgical resection. Only one study found that patients undergoing a right temporal lobe resection are at greater risk [6], but this has not been confirmed by others [8,10,30–32,34,35,38,39].

Significant preoperative risk factors for postoperative depression include: pre-existing history of affective disorders (depression or anxiety) [6,8,39,41]; fear auras [32]; temporal versus extra-temporal surgery [34]; and within this group, mesial versus lateral resections [8]. Females [42] and patients with poor psychosocial adjustment [31,34] or negative family dynamics [8] have also been found to be at higher risk. Due to methodological limitations, predictors of de novo depression could not be elucidated.

2.2. Anxiety

The prevalence of preoperative anxiety symptoms was also extremely variable, ranging from 0 to 48% [25,28–30,32–34,36,39,41,43,44], and as for depression, likely due to different methods used in diagnosing and measuring psychopathology. For instance, Devinsky et al. [39] reported that preoperatively a quarter of patients had moderate to severe anxiety according to scale data rating, whereas 17% met the clinical criteria for an anxiety disorder following a structured clinical interview (CIDI).

The majority of studies demonstrated reduced prevalence of anxiety postoperatively when assessed between 3 months and 12 years after surgery [5,28,33,39,43–45]. However, two studies [30,32] have suggested that anxiety symptoms may present early and resolve within the first few weeks following surgery. Ring et al. [30] reported that anxiety symptoms rose 6 weeks after TLE surgery in their surgical cohort and reduced to about half the pre-surgical prevalence rate by 3-month follow-up. Similarly, Wrench et al. [34] found that anxiety diagnoses peaked 4 weeks after temporal lobe surgery, remitting to pre-surgical levels 3 months later.

Four studies found an increase in the prevalence of anxiety disorders postoperatively [29,32,36,41], and one study demonstrated no significant change in self-reported anxiety symptoms [25].

Seven studies reported de novo anxiety cases, ranging from 3 to 26% [25,28,29,34–36,45]. The highest prevalence rate was noted one month after temporal lobe surgery (26%) [34].

Evidence for predictors of post-surgical anxiety indicates that patients with a previous history of affective disorders (depression/anxiety) [36,41] are more susceptible to postoperative anxiety. As with depression, TLE patients with preoperative fear auras were identified in one study as at greater risk of post-surgical anxiety disorders despite becoming seizure free [32].

Data relating to the predictive value of other clinical characteristics are unconvincing. Some authors have reported an association between temporal lobe (versus extra-temporal lobe) surgery and postoperative anxiety [34], but this has not been replicated [39]. There is conflicting evidence as to whether postoperative anxiety is influenced by seizure outcome. Two studies reported that anxiety disorders/symptoms were more common in patients with persistent seizures [32], or <50% reduction [26], but another study did not support such an association [39]. Of those studies considering surgical laterality, one reported an association between left temporal lobe resection and the development of de novo postoperative anxiety [30].

2.3. Interictal psychosis

The literature regarding interictal psychosis is dominated by case studies and these were excluded from this review. The reported preoperative prevalence rates are widely divergent (0–16%) [5,27,29,36,41,45,47,49,50]. Arguably, the high baseline prevalence of interictal psychosis may have been inflated by earlier retrospective studies that included patients directly referred for surgery from psychiatric institutions [5,45].

Patients with pre-existing interictal psychosis are often unlikely to be considered for surgical intervention for their seizures [5,27,36,41,45]. However, a recent small prospective study [50] found that positive symptoms (hallucinations/delusions) worsened for a subgroup of patients (n = 4/12) in the first 6 months and later improved to preoperative levels at 12-month follow-up. Negative symptoms (social withdrawal/emotional blunting) either persisted or remained unchanged in the majority of their patients at one-year follow-up. No patients with worsening psychotic symptoms required hospitalization.

There are a number of reports of an interictal psychosis presenting for the first time following TLE surgery [5,27,38,39,48,49,51]. Two prospective studies reviewed reported de novo interictal psychosis cases [38,39]. Blumer et al.'s [38] study of temporal and frontal resection cases demonstrated a 12% prevalence rate of de novo interictal psychosis at 6-month post-surgery. Notably, all de novo cases had undergone a temporal lobe resection. Devinsky et al.'s [39] uncontrolled study of temporal and frontal resections reported a much lower rate of de novo interictal psychosis (1.1%) at 24-month follow-up. It is possible that the de novo interictal psychosis prevalence rate may have been underestimated due to the high attrition rate of this study.