Long-term seizure, psychiatric and socioeconomic outcomes after frontal lobe epilepsy surgery

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LONG-TERM SEIZURE, PSYCHIATRIC AND SOCIOECONOMIC OUTCOMES AFTER FRONTAL LOBE EPILEPSY SURGERY

Abstract

Objective: Resective surgery for selected individuals with frontal lobe epilepsy can be effective, although multimodal outcomes are less established than in temporal lobe epilepsy. We describe long-term seizure remission and relapse patterns, psychiatric comorbidity, and socioeconomic outcomes following frontal lobe epilepsy surgery.

Methods: We reviewed individual data on frontal lobe epilepsy procedures at our center between 1990 and 2020. This included the presurgical evaluation, operative details and annual postoperative seizure and psychiatric outcomes, prospectively recorded in an epilepsy surgery database. Outcome predictors were subjected to multivariable analysis, and rates of seizure freedom were analyzed using Kaplan-Meier methods. We used longitudinal assessment of the Index of Multiple Deprivation to assess change in socioeconomic status over time.

Results: A total of 122 individuals with a median follow-up of seven years were included. Of these, 33 (27%) had complete seizure freedom following surgery, with a further 13 (11%) having only auras. Focal MRI abnormality, histopathology (focal cortical dysplasia, cavernoma or dysembryoplastic neuronal epithelial tumor) and fewer anti-seizure medications at the time of surgery were predictive of a favorable outcome; 67% of those seizure-free for the first 12 months after surgery never experienced a seizure relapse. Thirty-one of 50 who had preoperative psychiatric pathology noticed improved psychiatric symptomatology by two years postoperatively. New psychiatric comorbidity was diagnosed in 15 (13%). Persistent motor complications occurred in 5% and dysphasia in 2%. No significant change in socioeconomic deciles of deprivation was observed after surgery.

Significance: Favorable long-term seizure, psychiatric and socioeconomic outcomes can be seen following frontal lobe epilepsy surgery. This is a safe and effective treatment that should be offered to suitable individuals early.

Key words: extratemporal; comorbid; psychiatry; outcome

LONG-TERM SEIZURE, PSYCHIATRIC AND SOCIOECONOMIC OUTCOMES AFTER FRONTAL LOBE EPILEPSY SURGERY

INTRODUCTION

Surgery is an effective treatment for selected individuals with drug-resistant focal epilepsy. (1, 2) Most long-term outcome data relates to anterior temporal lobe resection, for which surgery is associated with 5-year seizure freedom rates of approximately 50%. (3) Studies of frontal lobe epilepsy surgery are usually in smaller cohorts and typically report seizure outcomes at individual time-points using single outcome measures, which may not capture postoperative seizure remission and relapse patterns. (4-8)

Seizure freedom is considered the most critical factor affecting the quality of life and employment following epilepsy surgery, but analysis of long-term socioeconomic outcomes has been constrained by a lack of standardized composite quality of life scores. (7, 9, 10) Several factors, including physical and psychiatric comorbidities following surgery, are likely to influence socioeconomic outcomes and quality of life, as well as seizure freedom. (11)

A better understanding of long-term seizure, psychiatric and socioeconomic outcomes will help inform discussions with individuals considering frontal lobe epilepsy surgery. Previous studies identified several factors associated with favorable outcomes after surgery, such as a focal abnormality on MRI, shorter duration of epilepsy and younger age at the time of surgery. (4-8) Some results are conflicting, with equally good outcomes between those with normal and abnormal MRI scans reported (1, 7, 12), and variable associations between duration of epilepsy and postoperative seizure freedom. (5) Further, the significance of factors such as needing intracranial EEG (icEEG) and extent of resection are less well defined in frontal lobe, as opposed to temporal lobe, epilepsy surgery. (5)

We describe long-term seizure outcome patterns, rates of psychiatric comorbidity and socioeconomic outcomes in a large cohort of individuals who underwent frontal lobe surgery for drug-resistant focal epilepsy at our center.

METHODS

We reviewed data from all individuals who had frontal lobe epilepsy surgery at the National Hospital for Neurology and Neurosurgery, London, UK, between February 1990 and December 2020. The data included prospectively collected preoperative data and annual updates on seizure type and frequency. Preoperative and contemporary records of each individual's current residential postcode are available in the database and double-checked against those held in the National Health Service (NHS) Digital Spine. Information for yearly updates was obtained from reviews of hospital records, supplemented by a direct annual inquiry by a data manager and neurologist.

Type and location of surgery was identified from operation records and postoperative MRI scans. Frontal resections were stratified into those that involved orbitopolar, frontomedial, dorsolateral and frontocentral regions. Operations were deemed extensive if they involved two or more of these regions. Resections were further stratified by gyral involvement, including adjacent regions such as the anterior cingulate cortex and insula. We only included data for the first procedure for those who had more than one surgical procedure.

This study was approved as a service evaluation into frontal lobe epilepsy surgery at University College London Hospitals (registration number 135-202021-SE). As a service evaluation posing no risk, individual informed consent was not required.

Seizure outcome

Seizure outcomes for each postoperative year were classified according to the International League Against Epilepsy (ILAE) surgery outcome scale.(13) Patterns of seizure remission and relapse following surgery were recorded to assess longitudinal seizure outcomes.(1) Those who discontinued anti-seizure medication (ASM) were recorded, as were the numbers and causes of death of those who died in the years following epilepsy surgery.

Psychiatric comorbidity

All individuals had structured preoperative interviews with a consultant neuropsychiatrist as part of the presurgical evaluation. At this interview, psychiatric diagnoses were recorded in accordance to Diagnostic and Statistical Manual of Mental Disorders (DSM) criteria. At our center, individuals also routinely undergo standardized postoperative neuropsychology and neuropsychiatry review at 6, 12 and 24 months. We reviewed electronic records of these encounters to identify rates of psychiatric comorbidity before and after surgery. Only active diagnoses, for which individuals were taking psychoactive medication (such as selective serotonin reuptake inhibitors) or had ongoing symptoms, were included for analysis.

Socioeconomic status

Since 2000, the Ministry of Housing, Communities & Local Government has published geographical measures of relative deprivation among 32,844 small areas of England, known as Lower Super Output Areas, each containing approximately 1,500 residents.(14) These areas are ranked by level of poverty, based on relative income, employment, education, health, disability, crime, housing and living environment. From these domains, an Index of Multiple Deprivation (IMD) is estimated, used as a marker of socioeconomic status in several studies, including previous work investigating differences in epilepsy prevalence among different regions of England.(15)

We matched postcode at time of surgery and last follow-up to Lower Super Output Areas within England. We referred to publicly available statistical releases to obtain decile ranks for each individual based on their residential postcode. Socioeconomic deciles were matched to demographic data from 2004, 2007, 2010, 2015 and 2019 to measure changes in socioeconomic status over time. We hypothesized that those who were seizure-free following surgery were more likely to experience IMD improvement than those with ongoing seizures.

To investigate whether those who had surgery had a different socioeconomic status from those who did not, we also compared deprivation deciles at the latest follow-up to an age, sex and duration of epilepsy matched cohort of individuals who completed presurgical evaluation for frontal lobe epilepsy but did not proceed to an operation. This comparison group was derived from a previous study of 617 consecutive individuals evaluated for epilepsy surgery at our center between January 2015 and December 2019, followed up for a median of 2.2 (IQR 1.3-3.2) years. (16, 17)

Statistical analysis

We compared the baseline characteristics of those with complete seizure freedom following surgery (outcome group pattern A1)(1) with those who were not completely seizure-free. We used the Kaplan-Meier method to estimate probabilities of remaining seizure-free for the entire postoperative duration. Exploratory univariate analysis was performed using Fisher exact, chi-square and Mann-Whitney U tests, for categorical and continuous outcomes, with a p-value

<0.05 deemed statistically significant. Significant covariates on univariate analyses were entered into a multivariable logistic regression model to assess predictors of favorable seizure outcome following surgery, with estimated odds ratios and associated 95% Confidence Intervals produced. A Bonferroni correction was performed to account for multiple comparisons when assessing levels of association between covariates and seizure freedom. We examined variables with a p<0.05 in the multivariable model as this was an exploratory analysis with a small number of significant covariates. The multivariable model was also adjusted for duration of follow-up to account for differing follow-up lengths between individuals. IBM SPSS Statistics for Windows v20 (International Business Machines Corp, Armonk, NY) was used for data analysis, with Kaplan-Meier curves created with MedCalc Statistical Software v20 (MedCalc Software Ltd, Ostend, Belgium; 2021).

RESULTS

Baseline characteristics

One hundred and twenty-two individuals had frontal lobe epilepsy surgery during the period. At the time of surgery, the median age was 33 (IQR 27-41) years, with a median duration of epilepsy of 20 (IQR 12-28) years. An abnormal MRI was seen preoperatively in 98 (80%) operated individuals. This included 75 (61%) with a focal abnormality such as focal cortical dysplasia (n=38), DNT (n=23) and cavernomas (n=14), and 23 (19%) with more diffuse abnormalities such as gliosis and encephalomalacia. Intracranial EEG recordings were undertaken in 70 (57%). Demographic and baseline preoperative characteristics of these individuals alongside a comparison group who completed evaluation but did not have surgery are provided in Table 1.

Reasons for people in the comparison group not proceeding to surgery included an inability to localize the epileptogenic zone (n=43), multifocal seizure onset (n=28), declining icEEG (n=11), declining surgery (n=9), risk of a post-surgical deficit (n=8) and co-existing neurological comorbidity (n=1).

Operation details

Of 122 surgeries performed, 37 (30%) were lesionectomies, and 85 (70%) were more extensive resections. There was an even distribution between left and right hemispheric resections. Frontomedial and dorsolateral resections were most common, followed by extensive lobectomies and orbitopolar resections. We were unable to access postoperative imaging in 15 (12%) people for detailed classification. Extrafrontal regions included with frontal resections were the anterior cingulate cortex in 31 (29%) and insular cortex in 8 (7%). The prefrontal cortex was the most common site of resection, with superior frontal gyrus resections in 34 (32%), middle frontal gyrus in 4 (4%), inferior frontal gyrus in 16 (15%) and combinations of the above in 52 (49%) cases. Focal cortical dysplasia (FCD) was the most common pathology identified, followed by dysembryoplastic neuroepithelial tumors (DNT) and cavernomas. Details are summarized in Table 2.

Surgical complications were seen in 34 (28%) individuals, including hemiparesis (14%), dysphasia (9%) and infection requiring antibiotics (7%). These operations included three extensive lobectomies and five dorsolateral resections. In most cases, neurological deficits resolved by three months; however, 6 (5%) had persistent weakness and 3 (2%) dysphasia. All instances of dysphasia were after left hemisphere resections.

Seizure outcomes

All included individuals had annual updates of seizure outcome for a minimum of 12 months. Twelve months after surgery, a total of 61 (50%) people were seizure free (ILAE outcome group 1 or 2). This dropped to 53 (44%) at the end of the second year and 47 (39%) at the end of the third postoperative year. Patterns of seizure relapse and remission, at last follow-up, are recorded in Table 3.

The median length of follow-up was 7 years (range 1-23 years). Of the entire cohort, 60 (49%) were seizure-free in the last 12 months of follow-up, of whom 33 (27%) had been seizure-free for the full duration of follow-up (outcome group pattern A1). A further 13 (11%) had only experienced auras postoperatively. At last follow-up, 14/122 (11%) people were no longer taking ASMs and all of these individuals were seizure-free.

Rates of long-term seizure freedom for different pathologies are listed in Table 4. The highest rate of seizure-freedom was seen in those with focal cortical dysplasia (47% seizure free), whereas none of the eight individuals who had no histopathological abnormality in the resected specimen experienced long-term seizure freedom. In the comparison group of people who completed presurgical evaluation for frontal lobe epilepsy but did not proceed to surgery, none of the individuals were seizure-free at a median follow-up of 2.2 (IQR 1.3-3.2) years.

We compared the preoperative findings, surgical resections and 12-month seizure outcomes between those who were completely seizure-free postoperatively (outcome group pattern A1) and those who were not (Table 5). On univariable analysis, taking less than four regular ASMs at time of surgery, a focal abnormality on MRI, and having focal cortical dysplasia on postoperative histology were associated with seizure freedom. On adjustment for multiple comparisons, only focal abnormality on MRI was statistically significant. Seizure freedom in the first 12 months was also a strong predictor of long-term outcome. Of 49 people seizure-free in the first 12 months postoperatively, 33/49 (67%) had sustained seizure freedom.
We included both focal abnormality on MRI and taking four or more ASMs into the multivariable logistic regression model, adjusted for duration of follow-up. Focal cortical

dysplasia was not included in the fitted model as this was highly correlated with focal abnormality on MRI. Compared to those taking less than four regular ASMs (n=96) at the time of surgery, those taking four or more regular ASMs (n= 26) were more likely to experience a seizure relapse (OR 4.71, 95% CI: 1.37-16.20) on multivariable analysis. Those who had a focal abnormality on MRI had a significantly higher chance of achieving sustained seizure freedom compared with those with diffuse pathologies or normal scans (OR 7.61, 95% CI: 2.66-21.74).

Four factors were associated with a significant difference in time to seizure relapse on log-rank testing of Kaplan-Meier plots (Figure 1). These were age at the time of surgery<30 years, taking less than four ASMs, presence of a focal MRI abnormality and the nature of the pathology. At the latest follow-up, ten (8%) had died, with four epilepsy-related deaths (two due to Sudden Unexpected Death in Epilepsy and two due to seizure-related injuries).

The monthly seizure frequency, presence of focal to bilateral tonic clonic seizures (FBTCS) or psychiatric pathology, and site or extent of resection did not significantly affect seizure outcome.

Neuropsychiatric outcomes

Before surgery, 50 (41%) individuals were being treated for psychiatric comorbidity. Diagnoses included major depression in 27 (22%), anxiety in 10 (8%), schizophrenia spectrum disorders in five (4%), behavioral disturbances in four (3%) and other diagnoses such as obsessive-compulsive disorder or post-traumatic stress disorder in the remaining four (3%). Four (3%) individuals had a history of probable non-epileptic seizures, and one person had been diagnosed with a dissociative disorder.

After surgery, 31/50 (62%) had remission of psychiatric symptoms at two years of follow-up. This group was significantly more likely to have experienced an improvement in seizure control, with seizures reduced by more than 50% baseline, within the first two years postoperatively (87% vs 63%, $p<0.05$).

Two-year follow-up data was available for 109 individuals. New psychiatric comorbidity was diagnosed, using contemporary DSM criteria, in 10 (8%) at 2-years follow-up (six new diagnoses of depression, three of anxiety and one of pathological aggression/behavioral disorder). Of these, 80% had ongoing seizures following surgery. There was no clear association between site or extent of resection and incidence of new psychiatric comorbidity after surgery. Rates of psychiatric diagnosis, including new diagnoses following surgery, are illustrated in Figure 2.

Socioeconomic outcomes

Nineteen (16%) of the cohort resided outside England and were excluded from the socioeconomic analysis. Four (3%) individuals were excluded as there was only 12 months of postsurgical follow-up information.

Consequently, 99 (81%) individuals were included in the socioeconomic analysis. The median Index of Multiple Deprivation (IMD) before surgery and at the latest follow-up was in the 5^{th} decile (i.e. residing in the 40-50% most deprived regions of England). The distribution of deprivation deciles before and after surgery is listed in Figure 3.

There was no association between having a seizure free outcome postoperatively and the preoperative IMD (Figure 3). Of those seizure-free, 20/40 (50%) did not move residence during the follow-up period. There was no significant difference in IMD at the latest follow-up between those who had epilepsy surgery and a matched cohort of individuals who completed presurgical evaluation but did not proceed to surgery. There was also no significant change in IMD from preoperatively to the latest follow-up comparing those who were seizure-free to those who were not.

Discussion

Long-term follow-up of individuals who underwent frontal lobe epilepsy surgery showed that a third were completely seizure-free after surgery, and more than half experienced at least one seizure-free year. These rates are consistent with previous reports and highlight the benefits of frontal lobe epilepsy surgery. (4, 7, 8)

We identified several predictors of complete seizure freedom postoperatively. The finding that those taking four or more ASM at the time of surgery were less likely to have prolonged seizure freedom has not been extensively explored and may be helpful to discuss with prospective surgical candidates. This does not infer that reducing the number of ASMs before surgery would improve outcomes. These individuals may have more widespread epileptic networks necessitating combination ASM, making them less likely to become seizure-free with surgery. In a study that considered the chance of people with drug-resistant epilepsy being offered surgery, a lower lifetime number of ASMs was associated with increased likelihood of physicians recommending resection. (18) A higher lifetime number of ASMs has previously been reported to be associated with a reduced chance of postoperative seizure-freedom (19), although this was in a mixed cohort of people who had temporal and extratemporal epilepsy surgeries. No significant relationship was identified between the average monthly number of seizures, the occurrence of FBTCS, site or extent of resection and the rate of postoperative seizure freedom, in contrast to other studies in which temporal lobe epilepsy predominates.(20)

Younger age at the time of surgery was associated with a more extended period of seizure remission, emphasizing the importance of offering surgery to suitable individuals earlier in life. This is consistent with data that suggest those with shorter epilepsy durations are more likely to be seizure-free at follow-up and underscores the importance of early referral to a surgical center.(21)

Having a focal abnormality on preoperative MRI was a favorable predictor for seizure freedom. In contrast to previous reports, intracranial EEG was not predictive of poor seizure outcome.(5, 22) This may reflect the selection of appropriate surgical candidates for and after icEEG, and demonstrates the utility of detailed preoperative investigation in those in whom the epileptogenic zone is unclear on imaging and scalp-EEG. Those who proceeded to surgery after accurate localization of the epileptogenic zone on icEEG had similar seizure freedom rates to those who did not need icEEG. This supports the concept that surgical outcome is more closely related to our ability to identify the epileptogenic zone rather than the specific investigations required for this identification.

Although numbers were small, none of the individuals who had undergone previous VNS experienced complete seizure-freedom after subsequent resective surgery. These people had often been considered for epilepsy surgery at earlier stages of presurgical evaluation before embarking on VNS while awaiting further multidisciplinary discussion or investigation. All these people had proceeded to icEEG prior to resective surgery. It is likely that these individuals were less optimal candidates for epilepsy surgery, for example due to difficulty identifying the epileptogenic zone, rather than VNS itself being a negative prognostic factor.

The underlying pathology was a strong predictor of favorable seizure outcomes. Those with focal pathologies, and in particular focal cortical dysplasia, had the highest rates of complete seizure freedom after surgery. Those with more diffuse pathologies such as gliosis, or who had no pathology identified in the resected specimen had the lowest rates of prolonged seizure freedom. There was no association between the size or extent of resection with seizure freedom. No association between resection site and incidence of psychiatric comorbidity was demonstrated.

One of the main factors limiting uptake of epilepsy surgery is the perceived risk of potential complications.(16) The persistent postoperative weakness or dysphasia rate was slightly higher than previous reports of approximately 2% significant complications with extratemporal epilepsy surgery.(23) This likely reflects the nature of our design in which even mild symptoms were actively sought and included, even if there was no significant functional impairment. Dysphasia was recorded if noted by treating physicians, and use of aphasia grading scales was not routinely recorded. The supplementary motor area (SMA) syndrome is a well-recognized transient disturbance of the ability to initiate voluntary motor and speech actions that may occur after dorsal superior frontal gyrus resections that usually resolve by 3 months. (24)

Epilepsy has long been associated with psychiatric comorbidity, considerably impacting quality of life.(25) Psychiatric diagnoses are up to three times as common in people with epilepsy when compared to the general population.(26, 27) Rates of depression and anxiety in our cohort were slightly lower than reported elsewhere(28), likely because we only included those on treatment or having active, ongoing symptoms. Most individuals experienced an improvement in psychiatric symptoms following surgery, with a smaller proportion developing new psychopathology. These new cases were usually linked to an absence of seizure freedom and likely reflected disappointment over a lack of benefit with surgery. Only one individual was diagnosed with a new behavioral disorder, with most new psychiatric diagnoses being depression or anxiety.

We have not reported upon changes in the neuropsychological profiles of our cohort. A previous study reported cognitive stability at a group level in thirty individuals two years after frontal lobe resection.(29) A decline in verbal reasoning ability was, however, commonly seen in those who had lateral and premotor/supplementary motor area resections. Further research delineating cognitive phenotypes and trajectories in people who have frontal lobe epilepsy surgery is required.

We did not find a significant difference in rates of seizure freedom between people of different preoperative socioeconomic status. This is consistent with other literature demonstrating no clear association between socioeconomic status and likelihood of a seizure-free surgical outcome.(30) Uptake of epilepsy surgery is, however, consistently less in people with lower socioeconomic status and these individuals often spend longer in presurgical evaluation.(16, 30) This highlights the need to address social and economic barriers to accessing epilepsy surgery in a universal healthcare system.

There was no significant improvement in IMD after surgery, even for those who became seizure-free. This could relate to the IMD being based on residential status, and half of those who became seizure-free postoperatively did not move during the follow-up period. Literature elsewhere investigating socioeconomic outcomes after surgery have yielded mixed results. It has been suggested that epilepsy surgery reduces hospital utilization rates but does not clearly correlate with better employment rates or a higher educational attainment.(31, 32) Other studies have shown epilepsy surgery is associated with higher levels of employment and positive psychosocial outcomes, particularly for those with seizure freedom.(32-35) There is marked heterogeneity between these studies, which are usually observational in nature, and with markers of socioeconomic status being variably defined.

There were several limitations to our study, which was confined to the experience of a single tertiary referral center, lacked controls and was retrospective. Three neurosurgeons carried out more than 90% of surgeries. The determination of seizure freedom was based upon self-reported outcomes, which may under- or overestimate seizure relapse rates, but is a real-life measure used in clinical practice. While residential postcodes can be used to approximate socioeconomic status in England, individual variations undoubtedly exist. The length of our follow-up nonetheless allowed us to evaluate long-term patterns of seizure remission in addition to a variety of other outcome measures which reflect real-world clinical data.

CONCLUSION

Frontal lobe epilepsy surgery is safe and effective. It should be offered to suitable individuals early, and having icEEG does not predict a poorer outcome. Approximately a third who have surgery will experience long-lasting seizure freedom, with another tenth only having auras. Rates of psychiatric comorbidity are lower following surgery and often resolve in those seizure-free.

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Ethical Publication Statement: We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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Table 1: Baseline preoperative characteristics of those who had frontal lobe epilepsy surgery		
Characteristic	**Surgical cases (n=122) (%)**	**Comparison group* (n=100) (%)**
Age of epilepsy onset, yr, median (IQR)	12 (6-18)	12 (6-17)
Age at surgery**, yr median (IQR)	33 (27-41)	33 (28-39)
Duration of epilepsy, yr, median (IQR)	20 (12-28)	21 (12-28)
Learning disability, n(%)	12 (10)	14 (14)
Prolonged early childhood convulsions, n (%)	5 (4)	4 (4)
Previous significant head injury, n (%)	9 (7)	4 (4)
History of focal to bilateral tonic clonic seizures, n (%)	94 (77)	74 (74)
History of status epilepticus, n (%)	17 (14)	14 (14)
Number of anti-seizure medications, median (IQR)	3 (2-3)	3 (2-4)
Psychiatric comorbidity, n (%)	50 (41)	38 (38)
Abnormal MRI, n (%)	98 (80)	35 (35)
Focal abnormality	75 (61)	25 (25)
Diffuse abnormality	23 (19)	10 (10)
FDG-PET performed, n (%)	37 (30)	76 (76)
Focal abnormality	15/37	44/76
icEEG performed, % with focal abnormality	70, 57%	11, 64%
Previous VNS, n (%)	8 (7)	16 (16)

*Individuals with FLE who entered the presurgical pathway but did not proceed to an operation

**In the comparison group this referred to age at the decision not to have surgery

Table 2: Operation details of frontal lobe epilepsy surgery	
Side of resection	**Number (%)**
Right	60 (49)
Left	62 (51)
Location of resection	
Orbitopolar	8 (7)
Frontomedial	35 (29)
Dorsolateral	42 (34)
Frontocentral	1 (1)
Extensive	21 (17)
Unknown	15 (12)
Postoperative complications	
Mono/Hemiparesis	
Transient (<3months)	11 (9)
Persistent (>3months)	6 (5)
Dysphasia	
Transient (<3months)	9 (7)
Persistent (>3months)	3 (2)
Infection (requiring antibiotics)	9 (7)
CSF leak	1 (1)
Pathology	
Focal cortical dysplasia	38 (31)
Type 2a	5/38
Type 2b	30/38
Unspecified	3/38
Dysembryoplastic neuroepithelial tumor	23 (19)
Cavernoma	14 (12)
Gliosis	14 (12)
Glioma**	13 (11)
No abnormality	8 (7)
Dual pathology	2 (2)
Other*	10 (8)

*Including Rasmussen's encephalitis (n=2), nonspecific abnormality (n=7) and gangliocytoma (n=1)

**Individuals were referred with drug-resistant epilepsy with a lesion subsequently found on MRI

Table 3: Seizure outcome group patterns (1) following epilepsy surgery		
OGP	**Description**	**N (%)**
A1	Completely seizure free since surgery	33 (27)
A2	Auras only since surgery	13 (11)
B	Seizures initially, then terminal remission	9 (7)
C	Initial seizure-freedom (>12 months) then relapse	10 (8)
D	Initial seizure-freedom, transient relapse, then terminal remission	3 (2)
E	Never seizure-free	46 (38)
F	Complex pattern of remissions and relapses	7 (6)
G	Information <1 yr or not enough information to categorize	1 (1)

Table 4: Rates of seizure freedom for different pathologies		
Pathology	**Number of cases, N (%)**	**Percentage seizure free for entire duration of follow-up (outcome group pattern A1)**
Focal cortical dysplasia	38 (31)	47%
Cavernoma	14 (11)	43%
Dysembryoplastic neuroepithelial tumor	23 (19)	39%
Low-grade glioma**		
Astrocytoma	8 (7)	33%
Oligodendroglioma	5 (4)	20%
Gliosis	14 (11)	14%
Dual pathology	2 (2)	0%
No abnormality in resected specimen	8 (7)	0%
Other*	10 (8)	10%

*Including Rasmussen's encephalitis (n=2), nonspecific abnormality (n=7), gangliocytoma (n=1)

**Individuals were referred with drug-resistant epilepsy with a lesion subsequently found on MRI

Table 5: Differences between those who did and did not have complete seizure freedom postoperatively				
Characteristic	**Seizure free (OGP A1), n=40**	**Not seizure free*, n=82**	**Odds Ratio (95% CI)**	**p**
Preoperative				
Age of epilepsy onset, yr, median (IQR)	12 (5-18)	12 (6-18)	0.97-1.05	0.65
Age at surgery, yr median (IQR)	30 (24-40)	36 (28-43)	0.99-1.07	0.08
Duration of epilepsy, yr, median (IQR)	19 (14-24)	21 (12-30)	0.99-1.06	0.22
Learning disability, n(%)	2 (5)	8 (10)	0.42-10.15	0.37
Prolonged early childhood convulsions, n (%)	1 (3)	4 (5)	0.22-18.50	0.53
History of focal to bilateral tonic clonic seizures, n (%)	28 (70)	66 (81)	0.74-4.22	0.2
History of status epilepticus, n (%)	3 (8)	14 (17)	0.69-9.41	0.15
More than 3 ASM, n (%)	4 (10)	22 (27)	0.10-0.95	**0.03**
Abnormal MRI, n (%)	35 (88)	63 (77)	0.16-1.38	0.16
Focal abnormality on MRI, n (%)	34 (85)	42 (51)	2.04-14.29	**<0.001**
icEEG performed, n (%)	19 (48)	51 (62)	0.85-3.90	0.12
Previous VNS, n (%)	0 (0)	8 (10)		
Index of Multiple Deprivation, median decile (IQR)	6 (4-9)	5 (3-8)	0.76-1.03	0.11
Psychiatric comorbidity	12 (30)	38 (46)	0.90-4.50	0.09
Operative				
Right sided resection, n (%)	19 (48)	41 (50)	0.43-1.93	0.8
Extensive resection, n (%)	7 (18)	14 (17)	0.36-2.63	0.95
Dorsolateral, n (%)	16 (40)	26 (32)	0.32-1.53	0.37
Frontomedial, n (%)	11 (28)	24 (29)	0.47-2.53	0.84
Orbitopolar, n (%)	1 (3)	7 (9)	0.43-30.65	0.24
Postoperative				
Seizure free in first 12 months after surgery	33 (83)	16 (20)	-	-
Focal cortical dysplasia	18 (45)	20 (24)	0.18-0.88	**.02**
Cavernoma	6 (15)	8 (10)	0.20-1.90	0.39
Dysembryoplastic neuroepithelial tumor	9 (23)	14 (17)	0.28-1.81	0.47
Low-grade glioma	4 (10)	9 (11)	0.32-3.85	0.87
Gliosis	2 (5)	12 (15)	0.69-15.31	0.12
No abnormality in resected specimen	0 (0)	8 (10)		0.05
*Includes individuals who experienced any postoperative seizures, including auras				

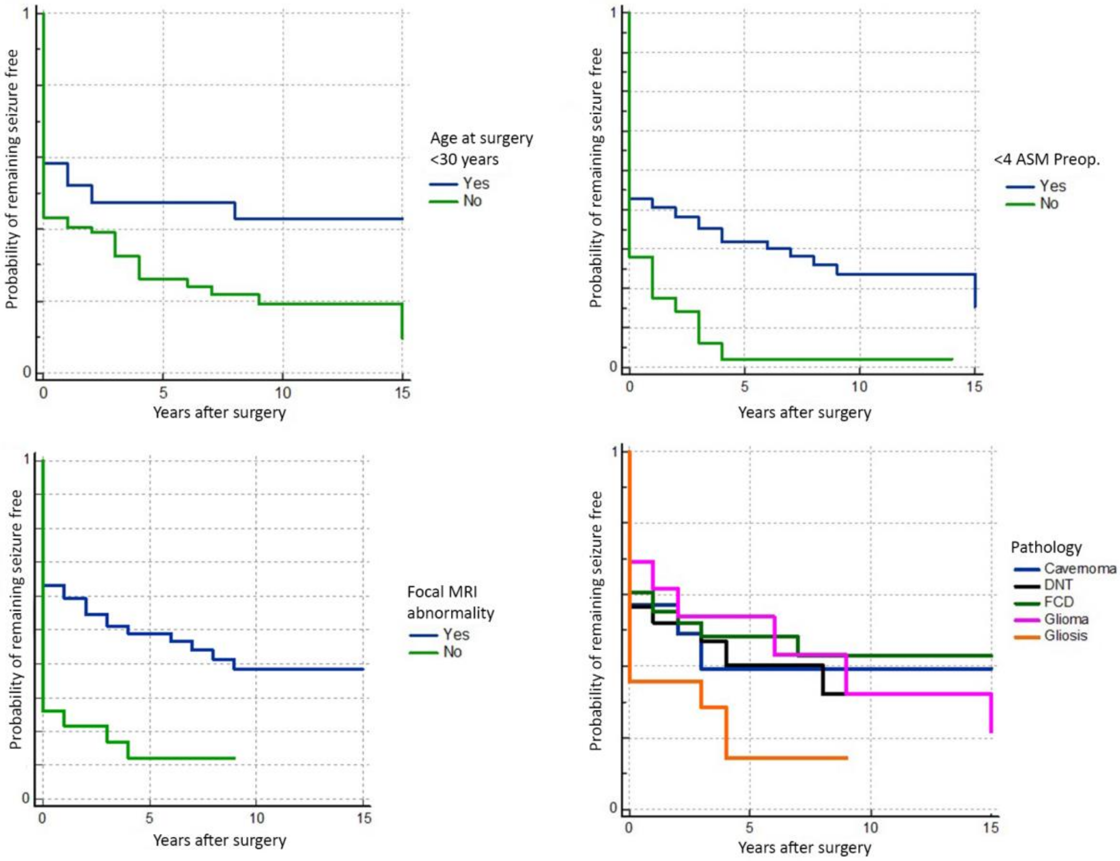

Figure 1: Kaplan-Meier curves for continuous seizure freedom after frontal lobe surgery

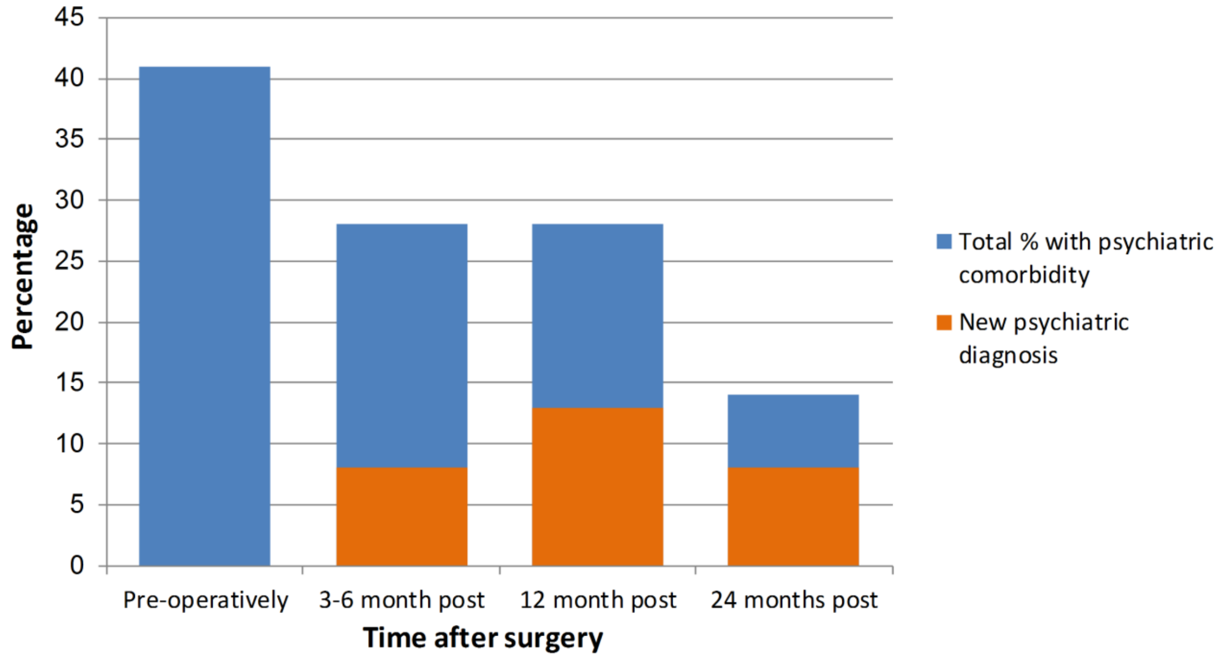

Figure 2: Rates of psychiatric comorbidity after surgery

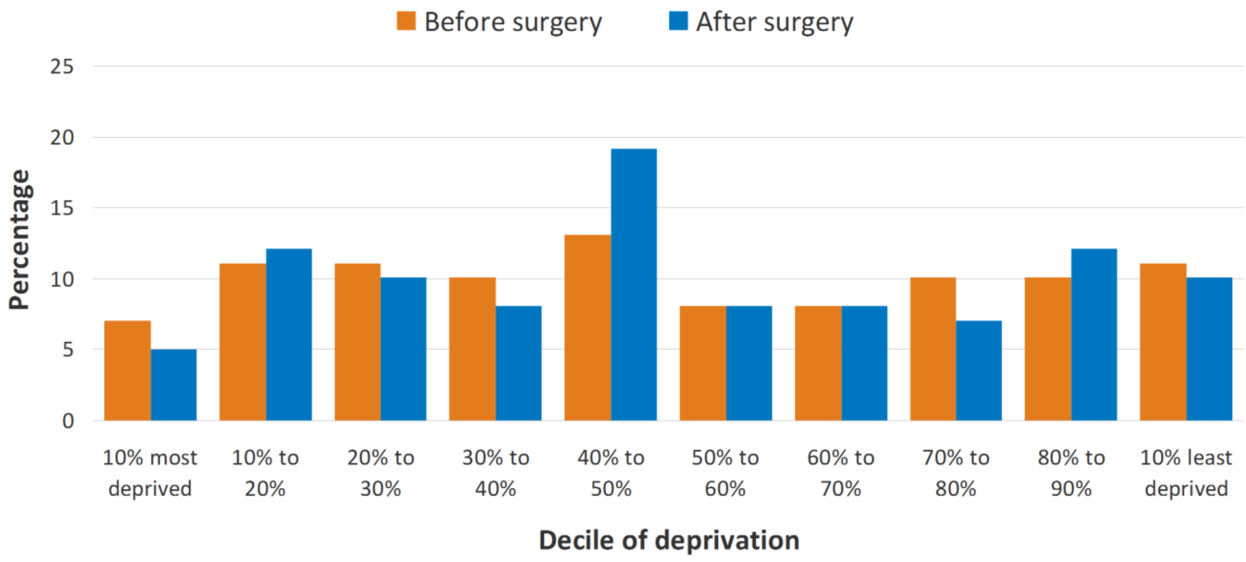

Figure 3: Distribution of deprivation deciles before and after surgery