Auras and the risk of seizures with impaired consciousness following epilepsy surgery: implications for driving

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Abstract

**Objective:** To calculate the chance of a seizure in the next year (COSY) for seizures with impaired awareness in those experiencing auras only, those with no seizures and those with continuing seizures.

Epilepsy surgery is an effective treatment for refractory focal epilepsy. Driving is an important factor affecting quality of life. In the UK, driving is not permitted if focal seizures with no impairment of awareness (auras, simple partial seizures) continue, if there is a prior history of seizures with impaired awareness, as will invariably be the case in those having epilepsy surgery. Current UK driving regulations allow driving if COSY is less than 20%.

**Method:** We calculated COSY in 819 epilepsy surgery patients with up to 25 years follow-up. Each patient year was graded on the ILAE epilepsy surgery outcome scale.

**Results:** Patients who were entirely seizure free for 1, 2 and 3 years had COSY of 4.9%, 3.5% and 2.4% respectively. Patients with only auras within the last 1, 2 or 3 years had a COSY of 11.3%, 9.2% and 7.8% respectively.

**Conclusions:** Individuals with auras only after epilepsy surgery had a higher COSY than those who were seizure free. If a COSY of below 20% is regarded as an acceptable risk, it may be suggested that those with auras only in a given year be allowed to drive. The relative risk of these patients causing accidents is lower than population groups such as those aged < 25 or > 75 years, who are permitted to drive.
Introduction

Neurosurgery is a successful treatment for medically intractable focal epilepsy.[1, 2] The International League against Epilepsy (ILAE) epilepsy surgery outcome scale provides six categories of seizure frequency which can be applied annually. Crucially, a distinction is made between those who are entirely seizure free, and those who have auras (focal seizures with retained awareness, simple partial seizures).[3]

After epilepsy surgery, patients have a dynamic range of outcomes, including prolonged remissions, remissions and relapses.[2] In this study 10% of patients continued to have auras following surgery. Driving is of great importance to individuals with epilepsy, and is a key benefit of seizure freedom.[4, 5] In the UK, the Driver and Vehicle Licensing Agency (DVLA) determines driving regulations. The most commonly applied rule is the need to be clear of seizures for one year to be eligible for a Group 1 licence (private motor car).

In the USA the required seizure free interval varies from state to state with restrictions ranging from 3 months to 12 months.[6] In Pennsylvania, an individual may drive providing a “specific prolonged aura accompanied by sufficient warning has been established over a period of at least 2 years immediately preceding, with or without medication”.[7] Some states, such as Indiana, have no set interval and an individual may drive so long as they are able to present a letter from a licenced physician stating they are taking effective medication.[8]

Currently in the UK, patients with auras (simple partial seizures, focal seizures without impairment of awareness) are permitted to drive if this pattern is established over 12 months, and if they have never had seizures which impaired awareness.[9] In an epilepsy surgical population it is highly unlikely for a patient to have never had a seizure with impaired consciousness. In consequence, post-surgical patients with continued auras do not qualify for a UK Group 1 driving licence.

Calculating Risk

The risk of epilepsy causing a driving accident depends on several factors. The chance of an occurrence of a seizure within the next year (COSY) is the expected seizure rate in a next given year and can be expressed as $C$. $R$ denotes the relative risk of a patient having an accident in comparison to unaffected members of the population. At present, the DVLA allows individuals to have a Group 1 licence if they are perceived to have a risk of seizure in the next year (COSY) of <20%. The following formula demonstrates the relationship between the COSY, relative risk ($R$) of a subject group compared with the overall driving population and other variables:[10, 11]

\[ C = (R-1) \times (F/DX) \]

$C$ = COSY

$R$ = Relative risk

$F$ = Present fatal casualty rate per driver per year

$D$ = Time spent behind the wheel

$X$ = Probability of a seizure at the wheel leading to a serious injury or fatality
The European Working Group on Epilepsy previously noted that individual risk, \( R \), is increased by many commonplace characteristics such as driver age >75yrs (\( R=3.2 \)) and male drivers <25yrs (\( R=7 \)).[11] These groups are permitted to drive and so it could be argued that other populations with \( R \leq 3 \) should also be allowed to drive.

Derivation of \( R \) using the above formulae with UK statistics is as follows. For a private driver, the time spent behind the wheel \( D \) is estimated at 4% of the average day, or 1 hour.[12] In Great Britain in 2014 there were 146,322 personal injury accidents reported to the police and 194,477 casualties (injuries of all severity).[13] Of the 194,477 casualties, 1,775 people were killed. There are currently 38,000,000 drivers with a full license in the UK (https://data.gov.uk/dataset/driving-licence-data). If 38,000,000 drivers cause 1,775 fatalities per year then the annual fatality rate, \( F \), would be roughly 1 fatality per 23,000 drivers (0.000044). \( X \) is the probability that a seizure whilst driving leads to a fatality. Approximately 60% of seizures behind the wheel lead to an accident.[11] \( X \) is therefore the chance an accident leads to a fatality (1,775/146,322) multiplied by 0.6 giving \( X=0.0073 \). It is possible that an accident caused by a seizure is more likely to lead to a fatality, but this is uncertain.[11, 14] Putting these values into the equation gives \( F/DX=0.15 \). Therefore, using our original equation, if \( C=0.2 \) (a 20% chance of a seizure within the next year) then \( R=2.33 \). If \( C=0.4 \) then \( R=3.67 \).

Thus, for the UK a 20% chance of a seizure within the next year would provide a relative risk, \( R \), of 2.33, a figure below the proposed \( R=3 \) and hence concordant with the DVLA policy of requiring a COSY below 20% in order to drive.

At present, the occurrence of auras only following surgery prohibits driving, as nearly all individuals will have had prior seizures with loss of consciousness. Approximately 10% of patients who have undergone epilepsy surgery continue to have auras only.[2] These patients are not currently allowed to drive in the UK. The risk of allowing these patients to drive has not been quantified. This study aimed to estimate the risks of this population having a seizure with impairment of consciousness in the following year and hence whether this population should be permitted to drive.

**Methods**

Data were collected from 950 operations on patients who had undergone epilepsy surgery at The National Hospital for Neurology and Neurosurgery between February 1990 and January 2014. Of these, 131 procedures were excluded (106 due to incomplete data or because surgery had taken place within the last 12 months and 25 as they were second operations in patients). Data were acquired from GP records, hospital notes and direct patient contact.

In total 819 patients were included. The number of post-operative years of follow-up per patient range from 2 to 25 (mean = 11.4 years, std. dev. = 6.2 years), with a total 9307 years of follow-up. Table 1 summarises characteristics of the patient cohort:
<table>
<thead>
<tr>
<th>Variable</th>
<th>Category</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Operation type</td>
<td>T Lob</td>
<td>633 (77.3%)</td>
</tr>
<tr>
<td></td>
<td>T Les</td>
<td>58 (7.1%)</td>
</tr>
<tr>
<td></td>
<td>Ex-T Lob</td>
<td>58 (7.1%)</td>
</tr>
<tr>
<td></td>
<td>Ex-T Les</td>
<td>49 (6.0%)</td>
</tr>
<tr>
<td></td>
<td>MST</td>
<td>3 (0.3%)</td>
</tr>
<tr>
<td></td>
<td>Hemi</td>
<td>14 (1.7%)</td>
</tr>
<tr>
<td></td>
<td>C Cal</td>
<td>4 (0.5%)</td>
</tr>
<tr>
<td>Side</td>
<td>Left</td>
<td>427 (52.0%)</td>
</tr>
<tr>
<td></td>
<td>Right</td>
<td>387 (47.3%)</td>
</tr>
<tr>
<td></td>
<td>N/A</td>
<td>6 (0.7%)</td>
</tr>
<tr>
<td>Pathology</td>
<td>HS</td>
<td>498 (60.8%)</td>
</tr>
<tr>
<td></td>
<td>GL</td>
<td>28 (3.4%)</td>
</tr>
<tr>
<td></td>
<td>CAV</td>
<td>51 (6.2%)</td>
</tr>
<tr>
<td></td>
<td>DNT</td>
<td>93 (11.4%)</td>
</tr>
<tr>
<td></td>
<td>FCD</td>
<td>36 (4.4%)</td>
</tr>
<tr>
<td></td>
<td>Dual Pathology</td>
<td>16 (2.0%)</td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td>97 (11.8%)</td>
</tr>
</tbody>
</table>

Table 1 – Cohort characteristics. Key: T Lob= Temporal lobectomy, T Les= Temporal lesionectomy, Ex-T Lob= Extra-temporal lobectomy, Ex-T Les= Extra-temporal lesionectomy, MST= Multiple subpial transection, Hemi= Hemispherectomy, C Cal= Corpus callosotomy, HS= Hippocampal sclerosis, GL= Glioma, CAV= Cavernoma, DNT= dysembryoplastic neuroepithelial tumour, FCD= focal cortical dysplasia.

Data were anonymised with each patient receiving a unique patient identifier. Information recorded for each patient included operation date, operation type, laterality of surgery, surgeon and neuropathology. For each year of follow-up the patient had been prospectively graded according to survival and the ILAE epilepsy surgery outcome scale (Table 2) regarding occurrence of seizures in the previous 12 months. Patients were followed up until either death or loss to follow-up. There were 34 patients (4.2%) who died during follow-up with various causes of death. Since the proportion of deaths in the cohort was small, mortality was not modelled explicitly. Data were analysed using Stata (version 14) for data summaries and R (version 3.1.3) for modelling.

<table>
<thead>
<tr>
<th>OUTCOME CLASSIFICATION</th>
<th>DEFINITION</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Seizure free, no auras</td>
</tr>
<tr>
<td>2</td>
<td>Simple partial seizures/auras only</td>
</tr>
<tr>
<td>3</td>
<td>One to three seizure days per year +/- auras</td>
</tr>
<tr>
<td>4</td>
<td>Four seizure days per year to a 50% reduction in seizure days per year +/- auras</td>
</tr>
</tbody>
</table>
Less than 50% reduction in seizure days to a 100% increase +/- auras

A more than 100% increase in seizure days +/- auras

Table 2 - The ILAE epilepsy surgery outcome classification.[3]

Principally, we considered ILAE grades 1 and 2, since any patient with ILAE grade ≥3 would not usually be permitted to drive (unless seizures only occurred during sleep for more than 3 years). As such, ILAE grades ≥3 are grouped together for the rest of this study.

Firstly, basic tables of the seizure variable aggregated across all years of follow-up, conditional on the past history of ILAE grade were produced. Estimates of the COSY were obtained together with 95% confidence intervals using a linear regression model. The confidence intervals did not account for the clustering of observations within patients.

To obtain marginal estimates of the probability of seizure occurrence, conditional on the past history of ILAE grade and accounting for the clustering of observations over time within patients, we used a generalised estimating equations (GEE) model with a binary outcome. Each GEE fit assumed an independence working correlation structure to avoid the possibility of bias in the model coefficient estimates.[15] Robust standard errors were used for the calculation of 95% confidence intervals to account for within-patient clustering.

Each model has the form:

\[ \log \left( \frac{p_{ij}}{1 - p_{ij}} \right) = \beta X_{ij} \]

With;

\[ p_{ij} = \text{Probability that patient } i \text{ undergoes a seizure in year } j. \]

\[ \beta = \text{Group of model coefficients to be estimated} \]

\[ X_{ij} = \text{Group of patient-specific covariates measured at time point } j. \]
## Results

Table 3: Risk of seizure with impaired awareness conditional on highest ILAE grade in previous 1, 2 and 3 years

<table>
<thead>
<tr>
<th>Previous year’s ILAE grade (n=819)</th>
<th>Seizure in year</th>
<th>Proportion of patients who have a seizure (95% confidence interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>1</td>
<td>237</td>
<td>4644</td>
</tr>
<tr>
<td>2</td>
<td>101</td>
<td>790</td>
</tr>
<tr>
<td>≥3</td>
<td>2380</td>
<td>336</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Highest ILAE grade in previous two years (n=770)</th>
<th>Seizure in year</th>
<th>Proportion of patients who have a seizure (95% confidence interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>1</td>
<td>143</td>
<td>3958</td>
</tr>
<tr>
<td>2</td>
<td>74</td>
<td>734</td>
</tr>
<tr>
<td>≥3</td>
<td>2237</td>
<td>523</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Highest ILAE grade in previous three years (n=724)</th>
<th>Seizure in year</th>
<th>Proportion of patients who have a seizure (95% confidence interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>1</td>
<td>84</td>
<td>3408</td>
</tr>
<tr>
<td>2</td>
<td>56</td>
<td>662</td>
</tr>
<tr>
<td>≥3</td>
<td>2055</td>
<td>634</td>
</tr>
</tbody>
</table>

Table 3 shows the proportion of patients who had a seizure with impairment of awareness in any given year, according to the previous year’s ILAE grade. Thus, for post-operative patients whose previous year ILAE grade=1, the estimated probability of a seizure in the next year (the COSY) was 0.049 or 4.9%. For those with ILAE outcome grades 1 and 2, there was progressively less risk of a seizure with loss of awareness, if the pattern was established for 2 or 3 years.

In view of within-patient clustering the GEE approach was used to estimate further COSY values for each group. We present three basic models for the marginal estimates of the probability of undergoing a seizure with impaired awareness in the following year.
Table 4: Simple generalised estimating equation model: Previous year’s ILAE grade

<table>
<thead>
<tr>
<th>Previous year’s ILAE grade</th>
<th>Estimated proportion of patients who undergo a seizure (95% confidence interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.049 (0.041, 0.057)</td>
</tr>
<tr>
<td>2</td>
<td>0.113 (0.091, 0.140)</td>
</tr>
<tr>
<td>≥3</td>
<td>0.876 (0.856, 0.894)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Highest ILAE grade in previous 2 years</th>
<th>Estimated proportion of patients who undergo a seizure (95% confidence interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.035 (0.029, 0.042)</td>
</tr>
<tr>
<td>2</td>
<td>0.092 (0.072, 0.116)</td>
</tr>
<tr>
<td>≥3</td>
<td>0.811 (0.782, 0.836)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Highest ILAE grade in previous 3 years</th>
<th>Estimated proportion of patients who undergo a seizure (95% confidence interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.024 (0.019, 0.030)</td>
</tr>
<tr>
<td>2</td>
<td>0.078 (0.060, 0.101)</td>
</tr>
<tr>
<td>≥3</td>
<td>0.764 (0.730, 0.795)</td>
</tr>
</tbody>
</table>

Table 4 also shows the risk of a seizure based on highest ILAE grade in the previous 2 and 3 years respectively. The results are similar to those in Table 3, but the 95% confidence intervals are slightly different, when accounting for the clustering within patients over time.

These models estimate overall, marginal, estimates of probabilities conditional on past ILAE grade history, but do not account for important patient-level covariates or possible changes over time. We therefore fitted GEE models that include ‘year’ (time in years since surgery) as a co-variate (Table 5), to account for the possibility of a linear trend over time. For these models, we report odds ratios together with associated 95% confidence intervals.

Table 5: Generalised estimating equation model with ILAE grade at previous year and years since surgery (year)

<table>
<thead>
<tr>
<th>Explanatory variable</th>
<th>Odds ratio*</th>
</tr>
</thead>
<tbody>
<tr>
<td>ILAE grade in previous year = 2</td>
<td>2.50 (1.87, 3.35)</td>
</tr>
<tr>
<td>ILAE grade in previous year ≥3</td>
<td>138.77 (106.41, 180.97)</td>
</tr>
<tr>
<td>Year</td>
<td>1.00 (0.99, 1.02)</td>
</tr>
</tbody>
</table>

*Odds ratio in comparison to the category: previous ILAE grade = 1.

The co-variate ‘year’ did not influence the likelihood of a disabling seizure (OR 1.00, 0.99-1.02). However, scoring ILAE grade 2 in a previous year does (OR 2.50, 1.87-3.35) as does a grade 3 or more in the previous year (OR 138.77, 106.41-180.97).

Current DVLA guidelines are predicated on the basis that patients who are seizure free for 1 year have a COSY below 20%. In our GEE model patients who were completely seizure free for 1 year had a 4.9% chance of a seizure with loss of awareness within the next 12 months.
A COSY of 4.9% would give an individual risk value of \( R = 1.33 \). Those with auras had a risk of 11.3% of such a seizure in the next year, giving an individual risk value of \( R = 1.75 \) (Table 6).

**Table 6: Individual risk based on previous year’s ILAE grade**

<table>
<thead>
<tr>
<th>Previous year’s ILAE grade</th>
<th>Relative risk, ( R )</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.33</td>
</tr>
<tr>
<td>2</td>
<td>1.75</td>
</tr>
<tr>
<td>≥3</td>
<td>6.84</td>
</tr>
</tbody>
</table>

**Discussion**

**Key findings**

The COSY for a patient with an ILAE grade 1 in any given year was estimated to be 4.9% with the upper bound of the 95% confidence interval less than 20%. This result supports current UK driving law, presuming the acceptable risk level is agreed upon. Current UK driving law holds that a COSY below 20% indicates an acceptable risk for driving. Patients with auras only in the previous 1 year had an estimated COSY of 11.3%, with an upper 95% CI of 14%. Risk was reduced if auras or simple partial seizures only had been present over the previous 2 or 3 years (9.2% and 7.8% respectively).

Patients with a seizure with loss of awareness in the previous year had an 87.6% risk of such a seizure in the next year, with a consequent relative risk of an accident of 6.84. It is notoriously difficult to be certain about the numbers of auras experienced by a patient as these usually occur at irregular intervals and frequency is not accurately recorded by individuals, so we cannot determine whether the frequency of recalled auras is a factor in predicting risk of a seizure with impairment of awareness. In clinical practice, on which decisions about driving are made, neurologists rely on the history provided by patients and witnesses to decide whether there is any impairment of awareness associated with reported brief focal seizures or auras. In general, auras do not occur at a frequency that would make video-EEG telemetry recordings a practical proposition.

If individual risk is considered, patients with grade 1 or grade 2 outcomes in any given year have a less than threefold risk of an accident (\( R = 1.33 \) and 1.75 respectively). These grades imply less of an increase in relative risk than increases associated with other characteristics that do not prevent driving such as age over 75, females <25 years and males <25 years (\( R = 3.1, 3.2 \) and 7 respectively).

**Implications for Driving Law**

Although patients with only auras have a raised COSY the increase is relatively small and these patients pose a similar risk to those who are entirely seizure free. The European
Working Group suggested that a COSY between 20% and 40% may be acceptable given the risks that drivers with other circumstances, both medical and biographical, may pose.

When other factors, such as the probability of a seizure occurring at the wheel and of a seizure with loss of awareness causing an accident are considered the overall increase in relative risk is small at 1.75 for the aura group and relatively low in comparison to other groups of drivers such as those aged <25 or >75 years. This risk estimate also relies on a number of assumptions such as driving for an average of 1 hour per day. The risk of a road traffic accident, and consequent injury, increases with the time spent driving. This is one of the reasons for the criterion for a Group 2 licence being a <2% annual risk of a seizure.

Given the significant potential improvements in quality of life and the relatively low individual risk increase in comparison to other groups an argument could be made that patients with auras only following epilepsy surgery could be considered safe enough to possess a group 1 driving licence.

Limited licences have been considered for epilepsy and are in place for other medical conditions.[11] Measures that could be considered include limiting time behind the wheel, banning the carriage of passengers, the avoidance of motorways and a 0% alcohol limit. These suggestions, however, would be difficult to police and may compromise the improvement in quality of life that patients expect.

Many medical conditions such as diabetes and heart disease increase the risk of an accident.[6] Problems may arise when, as is often the case, patients have multiple co-morbidities that individually may not exclude them from driving but together pose a potentially dangerous mix. Waller et al (1965) suggested that cardiovascular disease carries a 1.62 relative risk of an accident, diabetes 1.78 and substance abuse 2.8. The risk for patients with cardiovascular disease and diabetes, a common combination, is 2.88, higher than that of the aura only group in the current study.

In conclusion, using a simple generalised estimating equation we calculated the chance of a seizure with loss of awareness in the next year for multiple patient groups on the ILAE epilepsy surgery scale. Individuals having auras only after epilepsy surgery have a COSY of below the suggested 20% and a relative risk of 1.75. Given the improvements in quality of life that are possible through the liberalisation of driving law and the potential to reduce risk through limited licencing it may be reasonable to suggest that patients with auras only following epilepsy surgery be allowed to drive.

**Acknowledgements**

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