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Risk factors for postoperative depression in 150 subjects treated for drug-resistant focal epilepsy

Objective. The primary goal was to identify risk factors for post-surgical depression in subjects operated on for drug-resistant epilepsy. Secondary goals were to confirm the high rate of depression in subjects suffering from epilepsy (prior to surgery) and to look for first post-surgical depressive episode.

Methods. Case series study of 150 subjects surgically treated for partial epilepsy (side of surgery: 72 right, 78 left; site of surgery: 97 Unilobar Temporal, 17 Unilobar Frontal, 14 Posterior, 22 Multilobar). All subjects routinely had three psychiatric evaluations: before surgery (baseline) and at 6 and 12 months after surgery. Psychiatric diagnoses were made according to DSM-IV-TR criteria. Bivariate (Fisher exact test and Kruskal–Wallis rank sum test) and multivariate (logistic regression model fitting) analyses were performed.

Results. Thirty-three (22%) subjects had post-surgical depressive episodes, 31 of them in the first 6 months. Fourteen out of 33 experienced depression for the first time. Post-surgical depressive episodes are not associated with gender, outcome on seizures, side/site of surgical resection, histological diagnosis, psychiatric diagnoses other than depression. Depressive episodes before surgery and older age at surgery time are risk factors for post-surgical depression ($p = 0.0001$ and 0.01, respectively, at logistic regression analysis). No protective factors were identified.

Conclusions. Our data show that lifetime depressive episodes and older age at surgery time are risk factors for post-surgery depression. Moreover, a prospective study could be useful in order to assess whether depression is really a consequence of surgery.

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Key words: Depression, epilepsy surgery, risk factors.

Dear Editors

Introduction

The prevalence rate of depressive (up to 50%), anxiety (up to 25%) and psychotic disorders (up to 9%) is significantly higher in subjects with medically intractable epilepsy compared to general population and to patients with well-controlled seizures (Balabanov & Kanner, 2007).

Epilepsy surgery has become an established treatment for patients with medically intractable partial epilepsy (Choi *et al.* 2008).

Despite the relatively high prevalence of psychiatric comorbidity, a psychiatric evaluation is not routinely included in pre-surgical evaluation (Balabanov & Kanner, 2007; Pintor *et al.* 2007; Barry *et al.* 2008). Pre-surgical comorbid psychiatric disorders are relevant to epilepsy surgery because they could have an impact on seizures outcome, could influence post-surgical complications and the ability to adjust to a seizure-free life.

Post-surgical psychiatric complications mainly occur within the first 12 months of the surgery, with a higher incidence in the first 6 months (Balabanov & Kanner, 2007).

Studies on epilepsy surgery series have reported that between one-third and one-half of patients post-operatively develop for the first time in their lives, psychiatric symptoms (Balabanov & Kanner, 2007).

Correlation between psychiatric symptoms and site/side of surgery or post-surgical outcome is not consistent (Spencer *et al.* 2003; Wrench *et al.* 2004; Pintor *et al.* 2007).

Literature data on risk factors for post-surgical depression are controversial.

The primary goal of our study was to identify risk factors for post-surgical depression in subjects operated on for drug-resistant epilepsy. Secondary goals were to confirm the high rate of depression in subjects suffering from epilepsy (prior to surgery) and to look for the first post-surgical depressive episode.

Methods

Data collection

Since January 2002 to December 2007, a consecutive series of 150 adult subjects with epilepsy undergoing

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surgery for severe drug-resistant focal epilepsy were examined in this study (Engel *et al.* 1993).

Inclusion criteria: age range 18–60 years, focal medically intractable epilepsy.

Exclusion criteria: severe mental retardation.

Assessment

Psychiatric evaluation

All 150 subjects were assessed by a psychiatrist as a part of routine pre- and post-surgical assessment. The first psychiatric interview was conducted 1 week to 1 month before surgery.

The same psychiatrist, at the three evaluations, evaluated the same patients.

Diagnosis was made according to DSM-IV-TR criteria. We defined 'first depressive episode' as the first episode in lifetime before surgery, 'recurrent depression' in all the following episodes. The length of psychiatric follow-up was 12 months. Data about psychopharmachological therapies were collected at baseline, 6 and 12 months. The four depressed subjects at baseline were referred for treatment to psychiatric clinics near to their place of residence. Only one depressed subject accepted an antidepressant treatment as suggested by her psychiatrist. Subjects with post-surgical depression were referred for treatment to psychiatric clinics near to their place of residence. We did not analyze data on antidepressant therapies because of the small number of subjects.

Pre-surgical evaluation

All subjects were referred to the Epilepsy and Parkinson Surgery Centre 'C. Munari' at the Niguarda Hospital in Milan because of drug-resistant epilepsy. Surgery was performed after an individualized pre-surgical investigation (Talairach & Bancaud, 1973; Munari *et al.* 1994; Tassi *et al.* 2002; Cossu *et al.* 2005), adapted to the patient's anatomo-electro-clinical features. The site and extent of surgical resection were based on: neurological examination and history; neuroradiological (MRI, CT, Angiography) features; long-term video EEG monitoring. Fifty-seven were studied with long-term V-SEEG (Cossu *et al.* 2005).

At baseline, all patients were on antiepileptic (AE) politherapy.

Surgery. All the subjects received a tailored surgical resection aimed at removal of the epileptogenic zone, as defined by anatomo-electro-clinical data.

Post-surgical evaluation

Nearly all subjects continued the same (AE) therapy during the follow-up. Subjects were evaluated for outcome on seizures according to Engel's classification.

Statistical analysis

The outcome variable was the presence or absence of depressive episodes during the first 12 months after surgery.

Explanatory variables were gender, age at seizure onset, age at surgery, side and site of surgery, morpheic epilepsy, histological examination of the resected tissue, outcome on seizures, family history for psychiatric disorders, lifetime psychiatric diagnosis and psychiatric diagnosis at time of surgery.

Outcome on seizures was assessed according to Engel's classification (Engel *et al.* 1993).

The site of surgical resection was categorized as a multinomial variable: (I) unilobar temporal resections; (II) unilobar frontal resections; (III) posterior resections; (IV) multilobar resections (more than two lobes involved in the resection).

The bivariate analysis was propaedeutic, and the subsequent multivariate regression analysis was performed in order to develop risk factors for post-operative depressive episodes.

For bivariate analysis, Kruskal–Wallis rank sum test was used to analyze numerical variables, and Fisher's two-tailed exact test was performed to analyze categorical (binomial or multinomial) variables. The several tests of bivariate analysis were performed as an advanced preliminary inspection, and the obtained p-values were used in two ways: as a threshold ($p \leq 0.2$) to decide whether it was useful to test the explanatory variables into the multivariate model, and as a score to define their relative order into the regression model. For this reason, and because the general null hypothesis is not relevant to this study, no Bonferroni adjustment was made (Perneger, 1998).

For multivariate analysis, a logistic regression model (with Wald test) was fitted to assess the association of the explanatory variables with the outcome on depression in order to develop risk factors (Campbell 2006). The explanatory variables were selected with a multistep process, fitting some preliminary models and a final 'best' model. In order to avoid multicollinearity and variance inflation, the VIF (Fox, 2002) was every time computed (accepting VIF values <4), and the number of explanatory variables simultaneously included into the model never exceeded 3, because the events (post-surgical depressive episodes) were 33. Every variable potentially associated with the outcome (p-value at bivariate analysis >0.2) was sequentially added to the model, and the decision for the inclusion was taken according to the Best Subsets Technique (Fox, 2002) and performing an ANOVA test between the model with the considered variable and the nested model without it. So, the final model was fitted according to the results of this multistep process, as well as to the main evidences of the literature. Relative risk was calculated with the technique described by Zhang & Yu (1998).

$P < 0.05$ were considered as evidence of findings not attributable to chance.

Statistical analysis was performed using R2.8.1 (*R Development Core Team*, 2006).

Results

Thirty-three out of the 150 subjects (22%) had post-surgical depressive episodes, 31 in the first 6 months, and two in the last 6 months.

Explanatory variables *v*. outcome on post-surgical depression are shown in Tables 1 (categorical) and 2 (numerical), together with bivariate analysis results: statistically significant associations were found only for past depressive episodes and age at surgery.

Post-surgical depression was not associated with side/site of surgical resection, the presence of temporal mesial sclerosis and the presence of a depressive episode at baseline.

Seventy-four percent of subjects were seizure free (Engel's class I) at 12 months. Outcome on seizures was not significantly related to post-surgical depression.

Results of multivariate analysis are shown in Table 3.

The logistic regression model confirmed lifetime depression disorder and age at surgery as risk factors for post-surgical depression.

The site of surgery was included into the model, despite the fact that it is not associated with the outcome in our series, because of evidences from previous literature (Wrench *et al.* 2004; Pintor *et al.* 2007).

Relative risk analysis shows that one who has a personal history positive for depressive episodes has a risk for post-surgical depression 1.72 greater than others.

Twenty-nine subjects had at least a depressive episode in the past but were not depressed at baseline, three were depressed at baseline and had depressive episodes in the past, one was depressed only at baseline, for a total of 33 (22%) with depressive episodes sometimes before surgery.

After surgery, 14 subjects experienced depression for the first time in their life and nine of them were in Engel's class I.

Discussion

In our study, despite the good surgery outcome (74% Engel's class I), the percentage of subjects who were depressed during the 12 post-surgery months was higher than at baseline. Post-surgical depression is not significantly related to seizures outcome. The percentage of subjects with post-surgical depression in our study is consistent with studies in the literature and is significantly higher in those with a lifetime diagnosis of depression. Therefore, our results suggest that post-surgical depression is not significantly related to surgery outcome, but rather is strongly related to a history of previous episodes. Surgery could be a stressful event able to elicit a depressive episode in subjects at risk for depression.

Our findings are consistent with the literature on the high prevalence and incidence of depression in subjects with epilepsy (Barry et al, 2008). The most frequent psychiatric post-surgical complication is a depressive episode that develops within the first 12 months in 5–63% of subjects (Devinsky *et al.* 2005; Balabanov & Kanner, 2007). The relationship between post-surgical depression and seizures outcome is still an open question. Depression has been reported in subjects with good outcome as well as in subjects with unsatisfactory surgery outcome. In the Thapar *et al.* study (Thapar *et al.* 2005), depression score and seizure frequency were significant predictors for each other both within and across time. Depression in the Wrench *et al.* study (Wrench *et al.* 2004) did not seem to be related to seizure outcome, whereas Reuber *et al.* (2004) claimed that improvement in depression is related to seizure outcome. At baseline evaluation, the four subjects with depression were not on antidepressant therapy. The lack of antidepressant therapy in subjects with a depressive episode at baseline is consistent with published data that show that depression is both under-recognized and under-treated.

First depressive episode after surgery developed in 14 out of 150 (9.3%) subjects and was not related to post-surgical outcome. The percentage of first depressive episode after surgery in our study is lower than that reported in the literature (Preuter & Norra, 2005; Barry *et al.* 2008). In our study, we considered only the DSM-IV-TR depressive episodes, and therefore subjects with depressive symptoms not severe enough for a DSM-IV-TR diagnosis were not included.

In our sample, no significant relationship was found between depression and side of surgery (right *v*. left), site of surgery, mesial temporal sclerosis.

Published data show that most subjects who undergo surgery for medically intractable epilepsy have temporal localization (Cohen-Gadol *et al.* 2006). Quigg *et al.* (2003) found that right-sided epilepsy patients with pre-surgical depression may be particularly susceptible to post-surgical depression, but Wrench *et al.* (2004) have not confirmed a relationship between depression and temporal lobe epilepsy.

Table 1. *Categorical variables and outcome on post-surgical depression: results of the bivariate statistical analysis (two tails Fisher's exact text)*

Variable	Type	Categories	Frequencies (no. of cases)	Depression (%)		p-value
				Yes	No	
Sex	Binomial	Male	88	22.7	77.3	0.8
		Female	62	21.0	79	
Morpheic epilepsy	Binomial	Yes	14	14.3	85.7	0.46
		No	136	22.8	77.2	
Resection side	Binomial	Right	72	19.4	80.6	0.47
		Left	78	24.4	75.6	
Resection site	Multinomial	Temporal	97	21.6	78.4	0.44
		Frontal	17	29.4	70.6	
		Posterior	14	7.1	92.9	
		Multilobar	22	27.3	72.7	
Malformative pat.	Binomial	Present	84	20.2	79.8	0.56
		Absent	66	24.2	75.8	
Tumoral pat.	Binomial	Present	61	18.0	82	0.33
		Absent	89	24.7	75.3	
Flogistic – Degenerative pat.	Binomial	Present	7	28.6	71.4	0.67
		Absent	143	21.7	78.3	
Mesial temporal sclerosis	Binomial	Present	45	26.6	73.4	0.37
		Absent	105	20.0	80	
Criptogenic	Binomial	Present	10	40.0	60	0.15
		Absent	140	20.7	79.3	
Focal cortical displasias	Binomial	Present	80	20.0	80	0.53
		Absent	70	24.3	75.7	
DNT	Binomial	Present	10	40	60	0.15
		Absent	140	20.7	79.3	
Ganglioglioma	Binomial	Present	19	21.1	78.9	0.92
		Absent	131	22.1	77.9	
Outcome on seizures (Ia)	Binomial	Present	94	19.1	80.9	0.27
		Absent	56	26.8	73.2	
Psychiatric family history	Multinomial	Mood disorders	9	33.3	66.7	0.54
		Other disorders	6	33.3	66.7	
		Negative	135	20.7	79.3	
Psychiatric personal history						
Depression	Binomial	Present	32	50	50	0.00002*
		Absent	118	14.4	85.6	
Bipolar disorder	Binomial	Present	3	66.6	33,4	0.06
		Absent	147	21.1	78.9	
Anxiety disorder	Binomial	Present	11	0	100	0.07
		Absent	139	23.7	76.3	
Psychotic disorder	Binomial	Present	8	0	100	0.12
		Absent	142	23.2	76,8	
Anorexia nervosa	Binomial	Present	2	50	50	0.34
		Absent	148	21.6	78.4	
Impulse-control disorder	Binomial	Present	1	0	100	0.59
		Absent	149	22.1	77.9	
Dystimyc disorder	Binomial	Present	4	40	60	0.17
		Absent	146	21.2	78.8	
OCD	Binomial	Present	1	0	100	0.59
		Absent	149	22.1	77.9	
Hypochondriasis	Binomial	Present	1	0	100	0.59
		Absent	149	22.1	77.9	

Continued

Table 1. *Continued*

Variable	Type	Categories	Frequencies (no. of cases)	Depression (%)		*p*-value
				Yes	No	
Personality disorders (Cluster A)	Binomial	Present	4	0	100	0.28
		Absent	146	22.6	77.4	
Personality disorders (Cluster B)	Binomial	Present	9	11.1	88.9	0.42
		Absent	141	22.7	77.3	
Personality disorders (NOS)	Binomial	Present	6	0	100	0.18
		Absent	144	22.9	77.1	
Psychiatric diagnosis at pre-surgical evaluation						
Depression	Binomial	Present	4	50	50	0.17
		Absent	146	21.2	78.8	
Bipolar disorders	Binomial	Present	3	66.6	33.4	0.06
		Absent	147	21.1	78.9	
Anxiety disorders	Binomial	Present	11	0	100	0.07
		Absent	139	23.7	76.3	
Psychotic disorders	Binomial	Present	8	0	100	0.12
		Absent	142	23.2	76.8	
Personality disorders (Cluster A)	Binomial	Present	4	0	100	0.28
		Absent	146	22.6	77.4	
Personality disorders (Cluster B)	Binomial	Present	8	0	100	0.12
		Absent	142	23.2	76.8	
Personality disorders (Cluster C)	Binomial	Present	2	0	100	0.45
		Absent	148	22.3	77.7	
Personality disorders (NOS)	Binomial	Present	6	0	100	0.18
		Absent	144	22.9	77.1	
Impulse-control disorder	Binomial	Present	1	0	100	0.59
		Absent	149	22.1	77.9	
OCD	Binomial	Present	1	0	100	0.59
		Absent	149	22.1	77.9	
Dystimyc disorder	Binomial	Present	4	50	50	0.17
		Absent	146	21.2	78.8	
Hypochondriasis	Binomial	Present	1	0	100	0.59
		Absent	149	22.1	77.9	

*$p < 0.05$ were considered as evidence of findings not attributable to chance.
OCD: obsessive compulsive disorder.
DNT: Dysembryoplastic Neuroepihtelial Tumor.
NOS: Not Otherwise Specified.

Table 2. *Comparison of the considered numerical variables grouped by results, with bivariate statistical analysis (Kruskal–Wallis rank sum test)*

Variable	All patients median (IQ range)	Post-surgical depression		*p*-value
		Yes Median (IQ range)	No Median (IQ range)	
Age at seizures onset (years)	12 (5–17.75)	14 (8–18)	11 (4–17)	0.14
Duration of epilepsy (years)	20 (12–18.75)	21 (15–30)	19 (12–28)	0.31
Age at surgery (years)	33.5 (25.25–40.75)	38 (32–46)	32 (24–40)	0.008*
Monthly frequency of seizures (*n*)	10 (4–30)	10 (4–30)	10 (4–30)	0.56

*$p<0.05$ were considered as evidence of findings not attributable to chance.

Table 3. *Output of the fitted logistic regression models for, respectively, pre-surgical, surgical and post-surgical variables, with post-surgical diagnosis of depression (DSM-IV-TR) being the dependent variable*

				CI_{OR}			CI_{RR}		*p*-value
Variable	Category	Reference category	OR	2.5%	97.5%	RR	2.5%	97.5%	(Wald test) 0.000116*
Personal history for depression	Positive	Negative	6.06	2.45	15.53	1.72	1.42	1.88	
Age at surgery			1.05	1.01	1.09	–	–	–	0.014314*
Topography of resection	Frontal	Temporal	1.28	0.34	4.33	1.18	0.42	2.20	0.697154
	Posterior		0.17	0.01	1.15	0.18	0.01	1.14	0.125941
	Multilobar		1.80	0.53	5.70	1.48	0.61	2.51	0.325181

*$p<0.05$ were considered as evidence of findings not attributable to chance.

Thirty-one subjects became depressed after 6 months, only two after 12 months from surgery. These data are consistent with the literature, showing most frequent depression during the first six psychiatric complications, and data about risk factors are reported only in few studies (Balabanov & Kanner, 2007).

A positive personal history of depression is a risk factor for post-surgical depression in patients operated for drug-resistant partial epilepsy. Predicting which patients may experience depression after surgery is a challenge. Identification of those who are already depressed and need treatment for depression before surgery could be useful for reducing post-surgical depression. Our data suggest that subjects with a positive history for depression should be informed of a higher risk of developing a post-surgical depressive episode, also if they will have a good surgical outcome, in order to get adequate therapy as soon as possible.

Prospective studies should be designed in order to validate externally the logistic regression model we fitted, and to confirm (e.g. with a case-control analysis) that first depressive episodes are caused by surgery for epilepsy and not by major surgery in general.

Limits of the study:

(1) The psychiatric interview was a part of clinical routine assessment, and therefore we did not perform a standardized clinical interview. We are aware that the lack of a standardized research interview may limit the validity of diagnoses.
(2) Our study is not a prospective study
(3) By a statistical point of view, the evidence of the significant rule of positive personal history for depression and age at surgery as risk factors for post-operative depressive episodes is definitely stronger than the 'innocent' rule of the other analyzed variables. In fact, the major limit of this study, strictly related to the sample size and to the accepted α-error, is represented by the probably low power of the study. The formal computation of the β-error, variable by variable, could be very difficult, if not impossible, because of the weak and inhomogeneous evidences from the literature.
(4) The peculiarity of the sample does not allow one to generalize results for other population.

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Declaration of Interests

I.V.B., I.F.C., I.A.L., I.G.L.R., I.S.F., I.L.T., I.V.S., I.L.C., I.S.S. and I.O.G. declare full disclosure of any conflicts of interest.

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References

Balabanov AJ, Kanner AM (2007). Psychiatric aspects of epilepsy surgery. In *Psychiatric Issues I Epilepsy. A Practical Guide to Diagnosis and Treatment*, 2nd edn (ed. A. B. Etinger and A. M. Kanner), pp. 405–419. Lippincott Williams and Wilkins: Philadelphia.

Barry JJ, Ettinger AB, Friel P, Gilliam FG, Harden CL, Herman B, Kanner AM, Caplan R, Plioplys S, Salpekar J, Dunn D, Austin J, Jones J (2008). Consensus statement: the evaluation and treatment of people with epilepsy and affective disorders. *Epilepsy and Behaviour* **13**, S1–S29.

Campbell MJ (2006). Logistic regression. In *Statistics at Square Two*, 2nd edn (ed. M. J. Campbell), p. 35. Blackwell Publishing: Oxford.

Choi H, Sell RL, Lenert L, Muennig P, Goodman RR, Gilliam FG, Wong JB (2008). Epilepsy surgery for pharmacoresistant temporal lobe epilepsy: a decision analysis. *JAMA* **300**, 2548–50.

Cohen-Gadol AA, Wilhelmi BG, Collignon F, White JB, Britton JW, Cambier DM, Christianson JH, Marsh WR, Meyer FB, Cascino GD (2006). Long-term outcome of epilepsy surgery among 399 patients with nonlesional seizure foci including mesial temporal sclerosis. *Journal of Neurosurgery* **104**, 513–524.

Cossu M, Cardinale F, Castana L, Citterio A, Francione S, Tassi L, Benabid AL, Lo Russo G (2005). Stereoelectroencephalography in the presurgical evaluation of focal epilepsy: a retrospective analysis of 215 procedures. *Neurosurgery* **57**(4), 706–718.

Devinsky O, Barr WB, Vickrey BG, Berg AT, Bazil CW, Pacia SV, Langfitt JT, Walczak TS, Sperling MR, Shinnhar S, Spencer SS (2005). Changes in depression and anxiety after resective surgery for epilepsy. *Neurology* **65**, 1744–1749.

Engel J Jr., Van Ness P, Rasmussen T (1993). Outcome with respect to epileptic seizures. In *Surgical Treatment of the Epilepsies*, 2nd edn (ed. J. Engel Jr), pp. 609–621. Raven Press: New York.

Fox J (2002). Diagnosing problems in linear and generalized linear models. In *An R and S-Plus Companion to Applied Regression* (ed. J. Fox), pp. 191–233. Sage Publications, Inc.: Thousand Oaks, CA.

Munari C, Hoffmann D, Francione S, Kahane P, Tassi L, Lo Russo G, Benabid AL (1994). Stereo-electroencephalography methodology: advantages and limits. *Acta Neurologica Scandinavica* **152**(Suppl.), 56–67.

Perneger TV (1998). What's wrong with Bonferroni adjustments. *British Medical Journal* **316**, 1236–1238.

Pintor L, Bailles E, Fernandez-Egea E, Sanchez-Gistau V, Torres X, Carreno M, Rumia J, Matrai S, Boget T, Raspall T, Donaire A, Bargallo N, Setoain X (2007). Psychiatric disorders in temporal lobe epilepsy patients over the first year after surgical treatment. *Seizure* **16**, 218–225.

Preuter C, Norra C (2005). Mood disorders and their treatment in patients with epilepsy. *Journal of Neuropsychiatry and Clinical Neurosciences* **17**, 20–28.

Quigg M, Broshek DK, Heidal-Schultz S, Maedgen JM, Bertram EH III (2003). Depression in intractable partial epilepsy varies by laterality of focus and surgery. *Epilepsia* **44**, 419–425.

R Development Core Team (2006). *R: A Language and Environment for Statistical Computing*. R Foundation for Statistical Computing: Vienna, Austria. ISBN 3-900051-07-0 (http://www.R-project.org).

Reuber M, Andersen B, Elger CE, Helmstaedter C (2004). Depression and anxiety before and after temporal lobe epilepsy surgery. *Seizure* **13**, 129–135.

Spencer SS, Berg AT, Vckrey BG, Sperling MR, Bazil CW, Shinnar S, Langfitt JT, Walczak TS, Pacia SV, Ebrahimi N, Frbish D (2003). Initial outcomes in the multicenter study of epilepsy surgery. *Neurology* **61**(12), 1680–1685.

Talairach J, Bancaud J (1973). Stereotaxic approach to epilepsy. *Methodology of anatomo-functional stereotaxic investigations. Progress in Neurological Surgery* **5**, 297–354.

Tassi L, Colombo N, Garbelli R, Francione S, Lo Russo G, Mai R, Cardinale F, Cossu M, Ferrario A, Galli C, Bramerio M, Citterio A, Spreafico R (2002). Focal cortical displasia: neuropathological subtypes, EEG, neuroimaging ad surgical outcome. *Brain* **125**, 1719–1732.

Thapar A, Roland M, Harold G (2005). Do depression symptoms predict seizure frequency – or vice versa? *Journal of Psychosomatic Research* **59**, 269–274.

Wrench J, Wilson SJ, Bladin PF (2004). Mood disturbance before and after seizure surgery: a comparison of temporal and extratemporal resections. *Epilepsia* **45**, 534–543.

Zhang J, Yu KF (1998). What's the relative risk? A method of correcting the odds ratio in cohort studies of common outcomes. *JAMA* **280**, 1690–1691.