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Clinical determinants of psychopathological outcomes after epilepsy surgery

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ABSTRACT

Objectives: People with refractory epilepsy submitted to surgery may improve or deteriorate their cognitive and emotional functions. The aim of this study was to determine the predictors of longitudinal changes in psychopathological symptomatology, one year after epilepsy surgery, considering clinical and demographic characteristics.
Methods: People with refractory epilepsy referred to epilepsy surgery were included in this ambispective study. Psychiatric evaluations were made before surgery and one year after the procedure. Demographic, psychiatric, and neurological data were recorded. Linear regression was used to analyze longitudinal data regarding the Global Severity Index and 9 symptom dimensions of Symptom Checklist-90 (SCL-90).
Results: Seventy-six people were included. Bilateral epileptogenic zone, lack of remission of disabling seizures, and deep brain stimulation, targeting the anterior nucleus of the thalamus (ANT-DBS), were the most important predictors of an increase in SCL-90 scores, after surgery.
Conclusion: Some individual factors may have an impact on the development or worsening of the previous psychopathology. This study identifies clinical aspects associated with greater psychological distress, after surgery. These patients may benefit from more frequent psychiatric routine assessments for early detection.

1. Introduction

About one-third of people with epilepsy do not respond to adequate antiepileptic drug treatment [1]. These people are considered to have refractory epilepsy, a chronic and debilitating condition with a great impact on patients' quality of life [2,3].

Not surprisingly, previous studies have reported high rates of mental disorders and psychopathological symptoms in people with epilepsy, particularly in those suffering from refractory epilepsy [3–5]. The most commonly reported disorders are affective and anxiety syndromes [6,7].

Most people with refractory epilepsy display a well-characterized lesion considered to be the epileptogenic zone. Focal epilepsy affects, most frequently, the temporal lobe, particularly mesial structures – the hippocampus and the amygdala [6,7]. These people may be eligible for resective surgery, a procedure that is effective in the remission of seizures of about 70% of the cases [8]. For those whom, by any reason, surgical resection is not feasible, other options may be considered, namely, neuromodulation interventions, such as vagus nerve stimulation (VNS) or deep brain stimulation, targeting the anterior nucleus of the thalamus (ANT-DBS) [1].

Epilepsy surgery improves quality of life, even in those who are not seizure-free [9] plus may have a positive impact on the severity of depression, anxiety, and total psychiatric symptoms [10–12].

Previous studies, focusing on psychopathological dimensions after epilepsy surgery, have reported that psychiatric symptoms tend to decrease over time [10,13]. Although most patients seem to achieve a general improvement, others develop de novo psychopathology or may worsen their previous psychiatric condition [14]. In fact, epilepsy surgery has been associated with a high risk of mortality secondary to suicide [15]. Death from suicide occurs even after successful surgery in those people who became seizure-free [16].

Meldolesi et al. have shown a decrease of some state and trait emotional variables, as well as personality variables, such as interpersonal sensitivity, irritability, social introversion, and paranoia, at 1-year and 2-year follow-up evaluations, after surgery [13]. Similarly, Prayson et al. reported improvement in some subscales of the Personality Assessment Inventory that differed according to the surgical side and location, highlighting the importance of considering psychological changes according to patient's clinical characteristics [17].

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Table 1
Demographic and clinical characteristics of participants.

	Sociodemographical and clinical characteristics
Age, years	39.0 ± 11.7
Males, n (%)	28 (36.8)
Education, years	10.6 ± 4.5
Active workers, n (%)	41 (54.7)
Unemployed, n (%)	21 (28.0)
Retired, n (%)	13 (17.3)
Married, n (%)	37 (49.3)
Single or divorced, n (%)	38 (49.3)
Age at onset, years	17.2 ± 11.8
Duration of epilepsy, years	21.7 ± 14.1
Temporal epileptogenic zone, n (%)	63 (85.1)
Extratemporal epileptogenic zone, n (%)	7 (9.5)
Multilobar epileptogenic zone, n (%)	4 (5.4)
Side of the epileptogenic focus	
• Left	32 (42.7)
• Right	38 (50.7)
• Bilateral	5 (6.7)
Number of antiepileptic drugs	2.4 ± 0.6
Type of surgery, n (%)	
• Resective surgery	69 (90.8)
• Deep brain stimulation	7 (9.2)

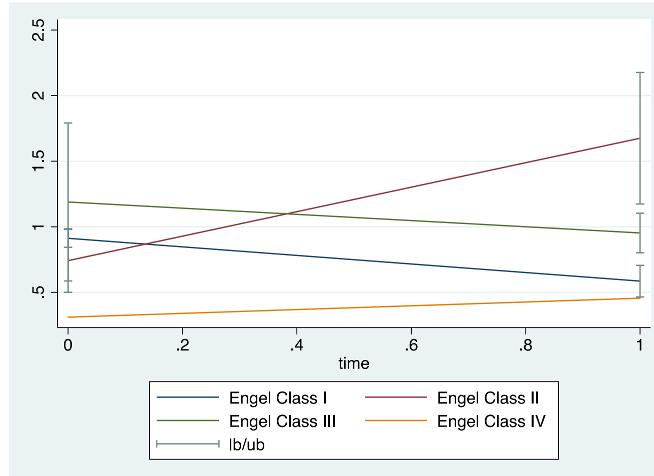

Fig. 2. Longitudinal changes in GSI, according to the Engel Class.

Regarding ANT-DBS, some studies suggest that it might have a positive impact on mood [18,19], while others found that it could worse depression scores [20,21]. The anterior nucleus of the thalamus has a critical position in the "Papez circuit", a group of brain regions with an important role on emotional and cognitive control. Deep brain stimulation, targeting the anterior nucleus of the thalamus may disrupt this circuit. It has been demonstrated that this procedure has deleterious effects on cognitive control and emotion–attention interaction [22]. Consequently, it may lead to dysfunctional mood and cognitive regulation, as well as, to an increased risk of psychopathological symptoms and psychiatric disorders.

While epilepsy surgery seems to have an impact on the psychopathological outcome, some authors suggested that presurgical psychopathology could also have an impact on the neurological outcome [23] suggesting a bidirectional relationship between these entities. However, a recent large cohort study by Altalib et al. did not confirm this association [24].

Despite the growing interest in psychopathology, both before and after surgery, there is a paucity of studies concerning the influence of different clinical features and surgical procedures on the postsurgical psychopathological symptoms of people with epilepsy. The purpose of this study was to address this issue.

2. Methods

This ambispective observational study was conducted at the Neurosciences' Department, of our institution, between February 2008 and October 2018. Retrospective and prospective data collection started after the study's approval by our Local Ethics Committee in 2015. Subjects were recruited consecutively from the Refractory Epilepsy Reference Center and the Epilepsy Surgery Group. The follow-up period was 12 months after surgery. Participants were evaluated by the psychiatrist belonging to both the Center and Group. The diagnosis of refractory epilepsy was made according to the definition of the International League Against Epilepsy [25].

Presurgical surgery evaluation, in our Group, includes, at least, a video electroencephalography (EEG) monitoring, a 3-Tesla brain magnetic resonance with an epilepsy protocol, and a neuropsychological and psychiatric evaluation. Most patients are submitted to resective surgery, a smaller proportion of them undergo ANT-DBS or VNS. Only patients submitted to resective surgery or deep brain stimulation (DBS) were enrolled in this study because of a lack of detailed follow-up data of patients submitted to VNS.

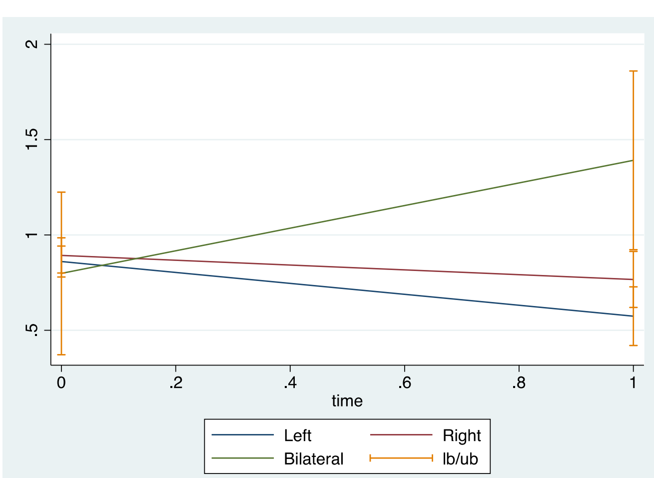

Fig. 1. Longitudinal changes in GSI, according to the epileptogenic zone side.

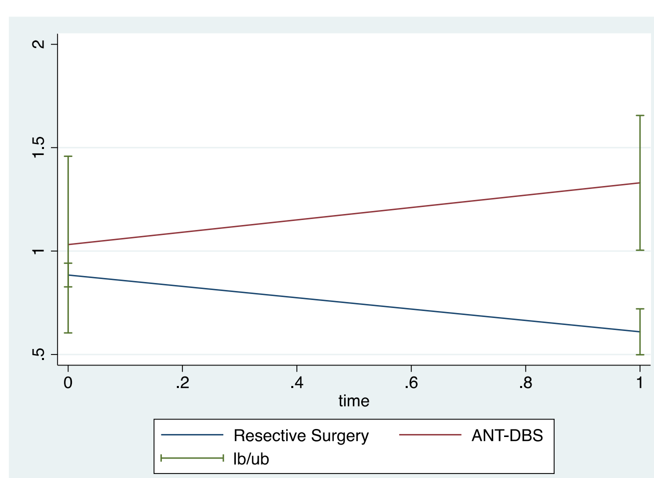

Fig. 3. Longitudinal changes in GSI, according to the type of surgery.

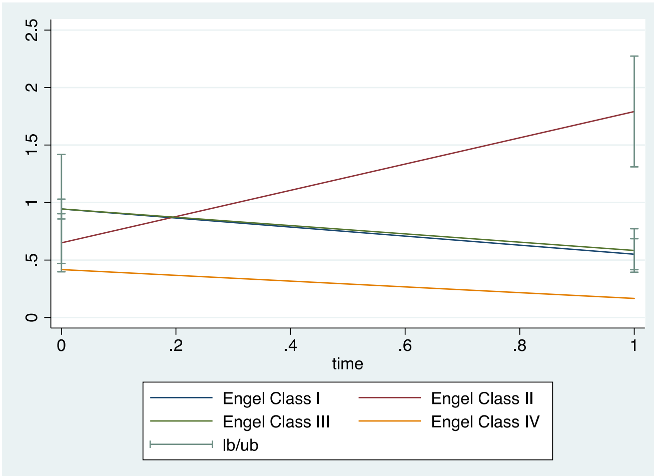

Fig. 4. Longitudinal changes in somatization subscale, according to the Engel Class.

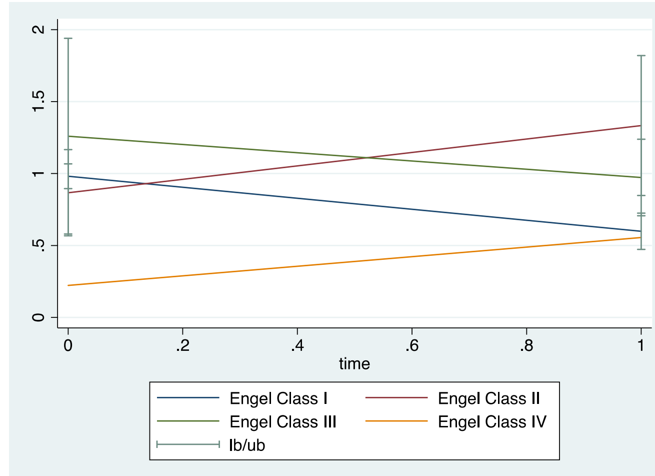

Fig. 6. Longitudinal changes in interpersonal sensitivity subscale, according to the Engel Class.

Demographic (gender, age, employment status, marital status) and clinical data (etiology of epilepsy, the topography of the epileptogenic zone, the age of onset, time to surgery, and Engel Class [26]), registered one month after surgery, were collected during interviews and from medical and surgical records. In the presurgical period, people were under, at least, two antiepileptic drugs, but their type and dosages were not addressed in this study because there was considerable variability between people, as it usually is in this population. However, in our center, people keep the same antiepileptic drugs and therapeutic schemes for at least 2 years after surgery.

A written consent form was obtained from participants evaluated prospectively, and the study was approved by the Local Ethics Committee.

2.1. Subjects

Participants older than 18, submitted to resective surgery or DBS, were included in this study. People with other neurological diseases or intellectual disability were excluded.

2.2. Psychiatric evaluation

Psychiatric evaluations were performed, before and 12 months after surgery, by one of the 3 psychiatrists from our group (LCP, FN, SL) and include a clinical psychiatric history (demographic data, previous psychiatric history, family history, use of substances as well as other relevant data) and Symptom Checklist-90 (SCL-90). This multidimensional instrument is a 90-item self-report symptom inventory developed to measure psychological symptoms and psychological distress. It has the following 9 subscales evaluating different symptom dimensions: somatization, obsessive–compulsive, interpersonal sensitivity, depression, anxiety, hostility, phobic anxiety, paranoid ideation, and psychoticism and a global scale called Global Severity Index (GSI) [27].

2.3. Statistical analysis

The statistical analysis was performed using Stata software (version 14.2; StataCorp, Texas, USA). Descriptive statistics were presented as mean ± standard deviation or as the number of subjects/cases and proportions.

A paired *t*-test was used to compare pre- and posttotal medium GSI scores.

For the longitudinal evaluation of SCL-90 subscales and GSI scores, after epilepsy surgery, as outcome variables, we performed linear regression. A set of predictor variables, clinically relevant both for epilepsy and psychiatric disorders, were included, as well as the SCL-90 baseline scores as a covariate.

Predictor variables include sex, age at surgery, duration of epilepsy, and age at onset of epilepsy, analyzed as continuous variables.

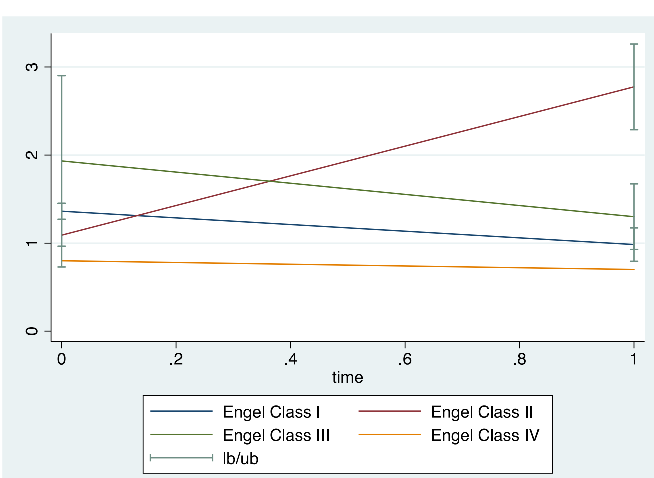

Fig. 5. Longitudinal changes in the obsessive–compulsive subscale, according to the Engel Class.

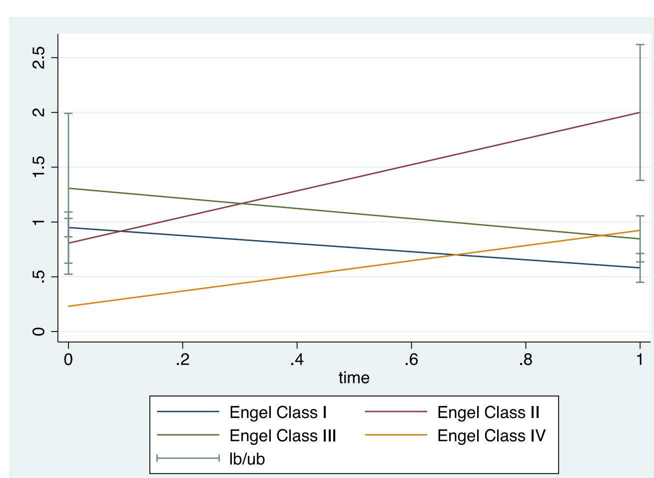

Fig. 7. Longitudinal changes in depression subscale, according to the Engel Class.

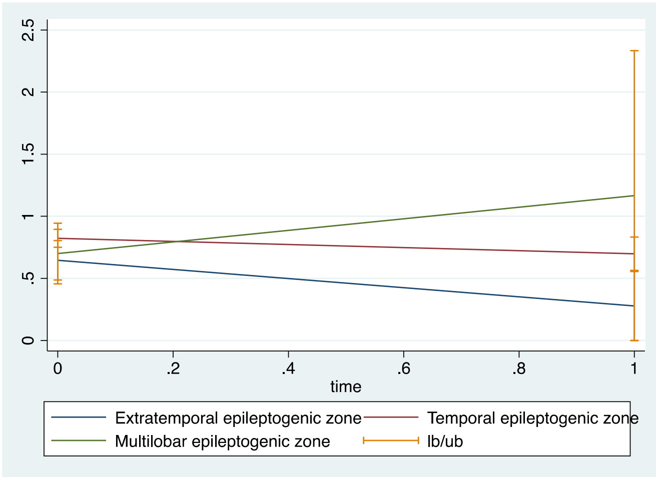

Fig. 8. Longitudinal changes in hostility subscale, according to the epileptogenic zone lobe.

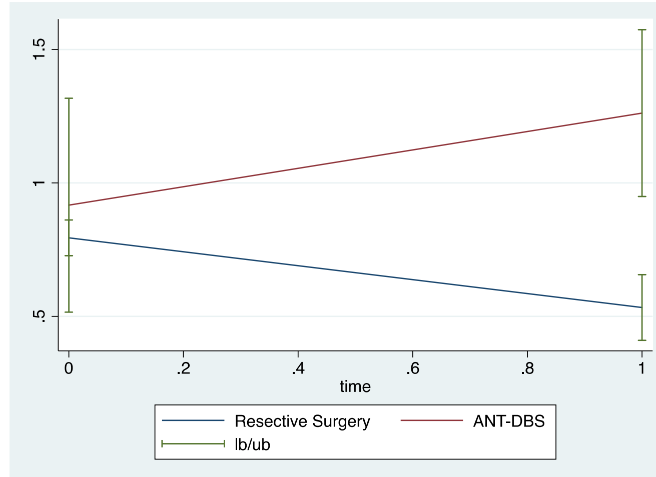

Fig. 10. Longitudinal changes in hostility subscale, according to the type of surgery.

Epileptogenic zone side (right, left, or bilateral cerebral hemispheres) and epileptogenic zone topography (temporal, extratemporal, or multilobar), and Engel Classes (I, II, III, or IV) [26] were analyzed as categorical variables. Mesial versus nonmesial temporal epileptogenic zone and resective surgery vs ANT-DBS were analyzed as binary variables.

Normality of residuals was tested for each model.

Measures of association were expressed as coefficients, and a p-value ≤0.05 was considered statistically significant.

3. Results

3.1. Demographic and clinical findings (Table 1)

One hundred and eight consecutive people with refractory epilepsy proposed to presurgical evaluation were enrolled. Ten were secondarily excluded because of intellectual disability (intelligence quotient [IQ] < 70), 18 because they did not undergo surgery, 2 because they underwent VNS; finally, 1 died and 1 refused to participate. Thus, a total of 76 individuals were included in the study.

Demographic and clinical characteristics are described in Table 1.

Sixty-three (85%) people had a temporal, 7 a frontal, and 4 an epileptogenic zone affecting more than one cerebral lobe. Regarding participants with temporal epilepsy, 35 (56%) had mesial sclerosis and 28 (35%) other pathologies.

One month after surgery, the outcomes of the majority of people (80%) were classified as Engel Class I.

3.2. Analysis of longitudinal changes in GSI of SCL-90 considering the total sample

At the presurgical and one-year evaluation, participants had a medium GSI score of 0.82 ± 0.61 and 0.82 ± 0.68, respectively. No significant differences were found considering the total sample.

3.3. Analysis of longitudinal changes in each SCL-90 symptom dimensions scores considering subgroups according to clinical predictors

Some subgroups of patients were found to have increased scores on some of the symptom dimensions and GSI, according to the defined predictors.

Figs. 1 to 17 represent all positive findings regarding longitudinal changes in SCL-90 subscales and GSI.

A summary of all positive findings has also been illustrated in Table 2.

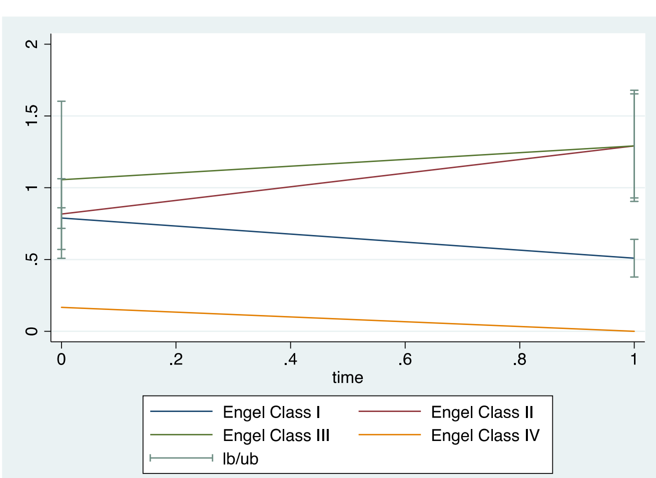

Fig. 9. Longitudinal changes in hostility subscale, according to the Engel Class.

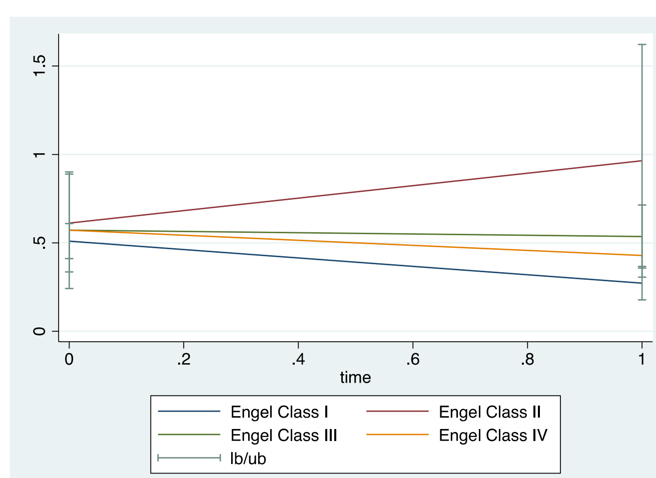

Fig. 11. Longitudinal changes in phobic anxiety subscale, according to the Engel Class.

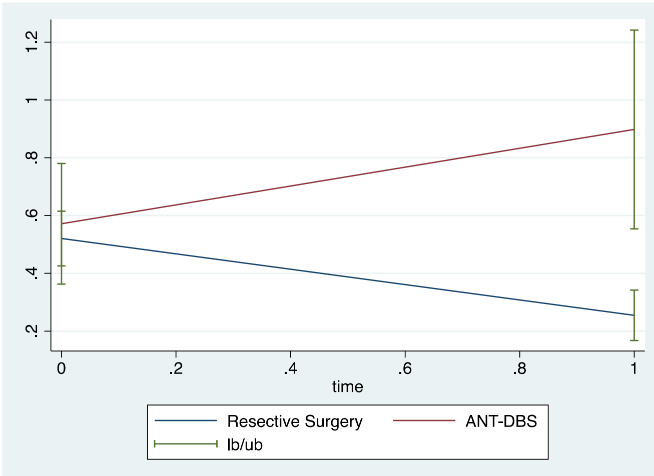

Fig. 12. Longitudinal changes in phobic anxiety subscale, according to the type of surgery.

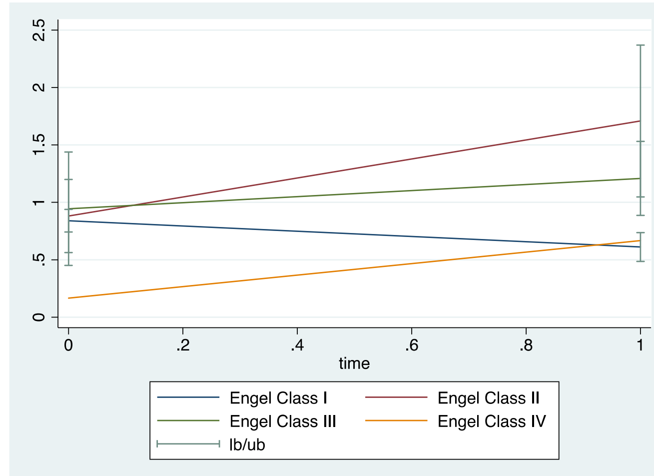

Fig. 14. Longitudinal changes in paranoid ideation subscale, according to the Engel Class.

4. Discussion

Considering the total sample, no significant differences were found regarding GSI, before and one year after surgery, although most of these patients have been free of seizures.

However, our study showed that some clinical factors may contribute to worse GSI scores, reflecting a postsurgery more severe general psychopathological profile in some subgroups of patients: those with a bilateral epileptogenic zone, those submitted to ANT-DBS, and those whose outcome was classified as Engel Class II.

Having an Engel Class II compared to Engel Class I was a predictor of higher scores one year after surgery, affecting all SCL-90 domains, as well as the GSI. These data are in line with previous studies showing an association between lack of seizure control after surgery and increased psychopathological symptoms [28,29].

Some hypothesis may explain this association, namely, the unmet expectations of patients and families. A mismatch between anticipated and real results, particularly, in those that do not become seizure-free, may lead to family and individual distress and frustration. Patients with seizure recurrence may become significantly disappointed or have a sense of "failure", these negative feelings may be reinforced by surgery complications or de novo psychiatric disorders [30,31].

Continued epileptogenic activity, after a major neurosurgical procedure, may also have a role in the increased psychological stress of patients without seizure remission. Abnormal electric activity may affect, directly or indirectly, brain circuits that have important roles in the control of emotions and cognition [28,29].

After surgery, a bilateral epileptogenic zone was associated with increased phobic anxiety and paranoid ideation scores whereas multilobar epileptogenic zone was associated with higher hostility scores.

These two characteristics could reflect more diffuse epileptogenicity, and are in accordance with previous findings, suggesting that a more generalized brain dysfunction could be associated with an increased risk for postoperative mental symptoms. Such findings also include a preoperative history of secondarily generalized tonic–clonic seizures [23], frontal hypometabolism in temporal lobe epilepsy [33], and preoperative bilateral independent spike discharges [28]. Dysfunctionality in different brain areas and circuits probably constitutes an important risk factor for the emergence of psychopathological symptoms after a major biological stressor such as epilepsy surgery.

Finally, the type of surgery, namely, being submitted to ANT-DBS in comparison to resective surgery, also contributed to the increased scores, after surgery, in the hostility, the phobic anxiety, and the paranoid ideation domains, as well as in the global scale. There are few studies reporting psychopathological outcomes after ANT-DBS for the treatment of refractory epilepsy. Findings include an increased risk of depression, paranoid, and anxiety symptoms after surgery [34,35]. It is

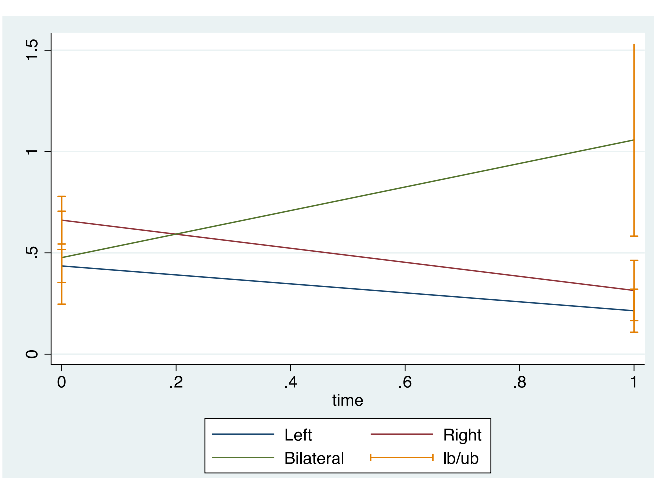

Fig. 13. Longitudinal changes in phobic anxiety subscale, according to the epileptogenic zone side.

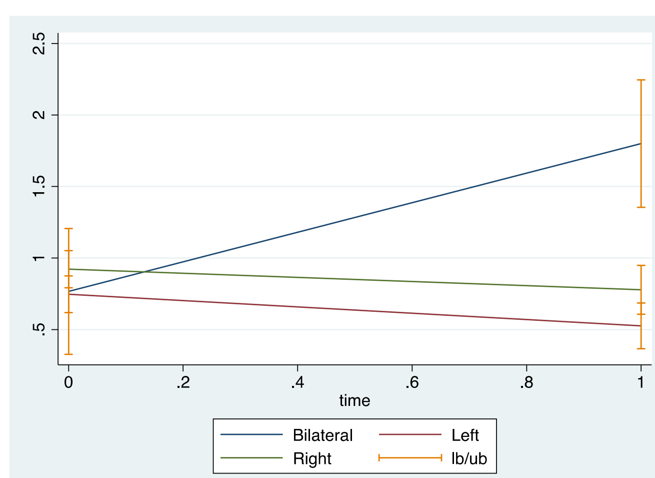

Fig. 15. Longitudinal changes in paranoid ideation subscale, according to the epileptogenic zone side.

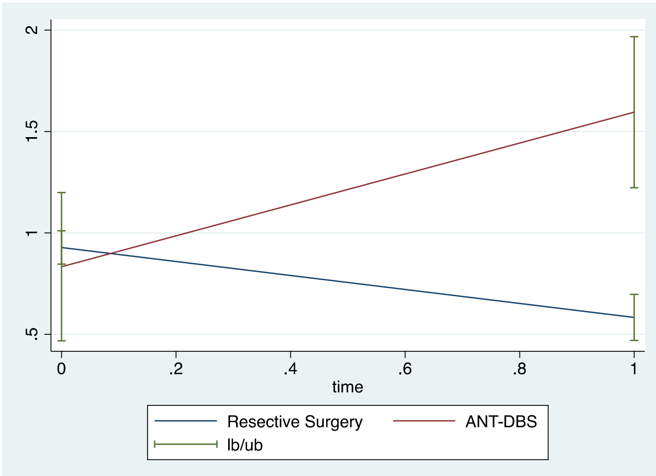

Fig. 16. Longitudinal changes in paranoid ideation subscale, according to the type of surgery.

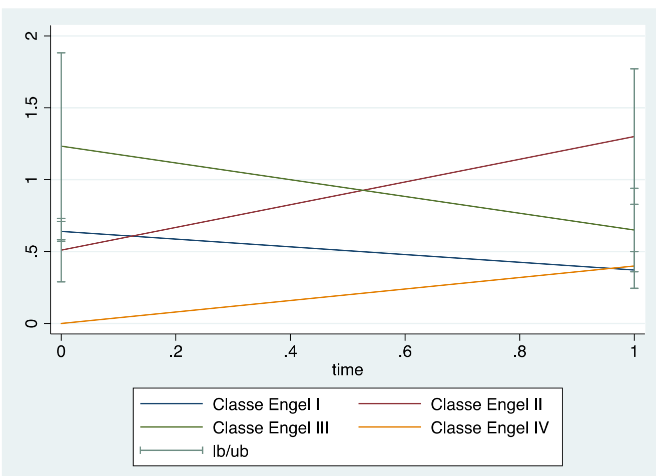

Fig. 17. Longitudinal changes in psychoticism subscale, according to the Engel Class.

uncertain into what extent this procedure may contribute to the disruption of important circuits involved in mood regulation.

A meta-analysis of psychiatric and neuropsychiatric adverse events associated with DBS, including different sites of stimulation, reported mixed findings regarding mood and behavior measured with the mentation, behavior, and mood (MBM) subscale of the unified Parkinson's disease rating scale. About half of the studies reported an improvement, 33% reported a worsening of symptoms and 11% reported no changes [36]. The fact that the majority of studies included in this analysis reported an improvement in psychopathological scores contrasts with our findings. However, this study includes many different stimulation sites and indications including depression and obsessive–compulsive disorder. Moreover, many of the studies did not report any outcomes regarding psychopathological outcomes. Interestingly, thalamus stimulation was associated with a higher risk of suicide, suggesting that this might be a particularly vulnerable structure [36]. Clearly, there is a need for further studies examining the psychopathological outcome after ANT-DBS.

This study has some limitations. The first is that this was an observational ambispective study with an important retrospective component. Missing information may introduce bias; however, different information sources were consulted to minimize the lack of data.

Epilepsy and psychiatric pharmacological treatments were not controlled and might have an impact on participant psychopathological symptoms. Nonetheless, all patients with clinically significant mental symptoms were referred to a psychiatrist and submitted to treatment. We do not expect that the predictors found in our models would influence the probability of being treated.

Finally, the sample size is relatively small, increasing the risk of a type II error.

Despite these constraints, important conclusions may be drawn from our study. Our findings suggest that the lack of complete seizure remission, more global epileptogenicity, and ANT-DBS are associated with more psychological distress after surgery. This research also offers some insights into what may constitute potential biological mechanisms involved in the development of psychiatric disorders and should be enhanced by prospective studies with more robust samples.

Conflict of interest

None.

Disclosure

The first author is responsible for data collection and integrity.

Funding sources

None.

Author's contributions

The study design was developed by FN and JP. Data collection was made by LCP, FN, MA, and SL. FN was responsible for data collection and data analysis and wrote the manuscript draft. LCP, JP, and MLF

Table 2
Summary of predictors of higher SCL-90 scores one year after surgery.

	Predictors of higher SCL-90 scores one year after surgery Coefficients (95% CI)			
	Engel Class II (compared to Engel Class I)	Bilateral epileptogenic zone	Multilobar epileptogenic zone	ANT-DBS
Somatization	1.32 (0.73,1.90)			
Obsessive–compulsive	1.62 (0.61,2.62)			
Interpersonal sensitivity	0.88 (0.11,1.65)			
Depression	1.60 (0.69,2.51)			
Hostility	0.77 (0.13,1.41)		0.82 (0.05,1.59)	0.59 (0.14,1.05)
Phobic anxiety	0.94 (0.18,1.71)	Left: 0.71 (0.03,1.38) Right: 0.73 (0.08,1.38)		0.62 (0.06,1.19)
Paranoid ideation	1.44 (0.66,2.23)	Left: 1.24 (0.55,1.94) Right: 1.06 (0.36,1.76)		1.17 (0.62,1.73)
Psychoticism	0.97 (0.22,1.73)			
Global Severity Index	1.19 (0.54,1.85)	Left: 0.65 (0.02,1.29) Right: 0.65 (0.02,1.28)		0.57 (0.02,1.11)

reviewed the manuscript draft. All authors have approved the final manuscript.

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References

[1] Gooneratne IK, Green AL, Dugan P, Sen A, Franzini A, Aziz T, et al. Comparing neurostimulation technologies in refractory focal-onset epilepsy. J Neurol Neurosurg Psychiatry 2016;87:1174–82.

[2] Kotwas I, McGonigal A, Bastien-Toniazzo M, Bartolomei F, Micoulaud-Franchi J-A. Stress regulation in drug-resistant epilepsy. Epilepsy Behav 2017;71:39–50. https://doi.org/10.1016/j.yebeh.2017.01.025.

[3] LM J, EJ O, Bo L, KE T, Christine C. Serious psychological distress among persons with epilepsy based on the 2005 California Health Interview Survey. Epilepsia 2009;50: 1077–84. https://doi.org/10.1111/j.1528-1167.2008.01996.x.

[4] Chang HJ, Liao CC, Hu CJ, Shen WW, Chen TL. Psychiatric disorders after epilepsy diagnosis: a population-based retrospective cohort study. PLoS One 2013;8:e59999. https://doi.org/10.1371/journal.pone.0059999.

[5] Hellwig S, Mamalis P, Feige B, Schulze-Bonhage A, van Elst LT. Psychiatric comorbidity in patients with pharmacoresistant focal epilepsy and psychiatric outcome after epilepsy surgery. Epilepsy Behav 2012;23:272–9. https://doi.org/10.1016/J.YEBEH.2011.12.001.

[6] Cascino GD. Surgical treatment for epilepsy. Epilepsy Res 2004;60:179–86. https://doi.org/10.1016/j.eplepsyres.2004.07.003.

[7] Caciagli L, Bernhardt BC, Hong S-J, Bernasconi A, Bernasconi N. Functional network alterations and their structural substrate in drug-resistant epilepsy. Front Neurosci 2014;8:411. https://doi.org/10.3389/fnins.2014.00411.

[8] BC J, GD C. Resective epilepsy surgery for drug-resistant focal epilepsy: a review. JAMA 2015;313:285–93.

[9] Hamid H, Blackmon K, Cong X, Dziura J, Atlas LY, Vickrey BG, et al. Mood, anxiety, and incomplete seizure control affect quality of life after epilepsy surgery. Neurology 2014;82:887–94. https://doi.org/10.1212/WNL.0000000000000183.

[10] Cunha I, Brissos S, Dinis M, Mendes I, Nobre A, Passão V. Comparison between the results of the Symptom Checklist-90 in two different populations with temporal lobe epilepsy. Epilepsy Behav 2003;4:733–9. https://doi.org/10.1016/j.yebeh.2003.09.002.

[11] Glosser G, Zwil A, Glosser D, O'Connor M, Sperling M. Psychiatric aspects of temporal lobe epilepsy before and after anterior temporal lobectomy. J Neurol Neurosurg Psychiatry 2000;68:53–8. https://doi.org/10.1136/jnnp.68.1.53.

[12] Ramos-Perdigués S, Baillés E, Mané A, Carreño M, Donaire A, Rumia J, et al. A prospective study contrasting the psychiatric outcome in drug-resistant epilepsy between patients who underwent surgery and a control group. Epilepsia 2016;57: 1680–90. https://doi.org/10.1111/epi.13497.

[13] Meldolesi GN, Di Gennaro G, Quarato PP, Esposito V, Grammaldo LG, Morosini P, et al. Changes in depression, anxiety, anger, and personality after resective surgery for drug-resistant temporal lobe epilepsy: a 2-year follow-up study. Epilepsy Res 2007;77:22–30. https://doi.org/10.1016/j.eplepsyres.2007.08.005.

[14] Iranzo-Tatay C, Rubio-Granero T, Gutierrez A, Garcés M, Conde R, Gómez-Ibáñez A, et al. Psychiatric symptoms after temporal epilepsy surgery. A one-year follow-up study. Epilepsy Behav 2017;70:154–60. https://doi.org/10.1016/J.YEBEH.2017.02.029.

[15] Pompili M, Girardi P, Ruberto A, Tatarelli R. Suicide in the epilepsies: a meta-analytic investigation of 29 cohorts. Epilepsy Behav 2005;7:305–10. https://doi.org/10.1016/j.yebeh.2005.05.010.

[16] Hamid H, Devinsky O, Vickrey BG, Berg AT, Bazil CW, Langfitt JT, et al. Suicide outcomes after resective epilepsy surgery. Epilepsy Behav 2011;20:462–4. https://doi.org/10.1016/j.yebeh.2010.12.031.

[17] Prayson BE, Floden DP, Ferguson L, Kim KH, Jehi L, Busch RM. Effects of surgical side and site on psychological symptoms following epilepsy surgery in adults. Epilepsy Behav 2017;68:108–14. https://doi.org/10.1016/j.yebeh.2016.11.004.

[18] Salanova V, Witt T, Worth R, Henry TR, Gross RE, Nazzaro JM, et al. Long-term efficacy and safety of thalamic stimulation for drug-resistant partial epilepsy. Neurology 2015;84:1017–25. https://doi.org/10.1212/WNL.0000000000001334.

[19] Chan AY, Rolston JD, Rao VR, Chang EF. Effect of neurostimulation on cognition and mood in refractory epilepsy. Epilepsia Open 2018;3:18–29. https://doi.org/10.1002/epi4.12100.

[20] Tröster AI, Meador KJ, Irwin CP, Fisher RS. Memory and mood outcomes after anterior thalamic stimulation for refractory partial epilepsy. Seizure 2017;45: 133–41. https://doi.org/10.1016/j.seizure.2016.12.014.

[21] Fisher R, Salanova V, Witt T, Worth R, Henry T, Gross R, et al. Electrical stimulation of the anterior nucleus of thalamus for treatment of refractory epilepsy. Epilepsia 2010; 51:899–908. https://doi.org/10.1111/j.1528-1167.2010.02536.x.

[22] Hartikainen KM, Sun L, Polvaara M, Brause M, Lehtimäki K, Haapasalo J, et al. Immediate effects of deep brain stimulation of anterior thalamic nuclei on executive functions and emotion-attention interaction in humans. J Clin Exp Neuropsychol 2014;36:540–50. https://doi.org/10.1080/13803395.2014.913554.

[23] Cleary RA, Thompson PJ, Fox Z, Foong J. Predictors of psychiatric and seizure outcome following temporal lobe epilepsy surgery. Epilepsia 2012;53:1705–12. https://doi.org/10.1111/j.1528-1167.2012.03604.x.

[24] Altalib HH, Berg AT, Cong X, Vickrey BG, Sperling MR, Shinnar S, et al. Presurgical depression and anxiety are not associated with worse epilepsy surgery outcome five years postoperatively. Epilepsy Behav 2018;83:7–12. https://doi.org/10.1016/j.yebeh.2018.01.040.

[25] Kwan P, Arzimanoglou A, Berg AT, Brodie MJ, Allen Hauser W, Mathern G, et al. Definition of drug resistant epilepsy: consensus proposal by the ad hoc Task Force of the ILAE Commission on Therapeutic Strategies. Epilepsia 2009;51:1069–77. https://doi.org/10.1111/j.1528-1167.2009.02397.x.

[26] Thaddeus W. Surgical treatment of the epilepsies, ed 2. Edited by Jerome Engel, Jr, New York, Raven Press, 1993, 786 pp, illustrated, $135.00. Ann Neurol 2018;35: 252. https://doi.org/10.1002/ana.410350236.

[27] Ruis C, van den Berg E, van Stralen HE, Huenges Wajer IMC, Biessels GJ, Kappelle LJ, et al. Symptom Checklist 90–Revised in neurological outpatients. J Clin Exp Neuropsychol 2014;36:170–7. https://doi.org/10.1080/13803395.2013.875519.

[28] Anhoury S, Brown RJ, Krishnamoorthy ES, Trimble MR. Psychiatric outcome after temporal lobectomy: a predictive study. Epilepsia 2000;41:1608–15.

[29] Metternich B, Wagner K, Brandt A, Kraemer R, Buschmann F, Zentner J, et al. Preoperative depressive symptoms predict postoperative seizure outcome in temporal and frontal lobe epilepsy. Epilepsy Behav 2009;16:622–8. https://doi.org/10.1016/j.yebeh.2009.09.017.

[30] Wilson SJ, Bladin PF, Saling MM. The burden of normality: a framework for rehabilitation after epilepsy surgery. Epilepsia 2007;48:13–6. https://doi.org/10.1111/j.1528-1167.2007.01393.x.

[31] Novais F, Pestana LC, Loureiro S, Andrea M, Figueira ML, Pimentel J. Predicting de novo psychopathology after epilepsy surgery: a 3-year cohort study. Epilepsy Behav 2019;90:204–8. https://doi.org/10.1016/j.yebeh.2018.11.037.

[32] Salzberg M, Taher T, Davie M, Carne R, Hicks RJ, Cook M. Depression in temporal lobe epilepsy surgery patients: an FDG-PET study. Epilepsia 2006;47:2125–30. https://doi.org/10.1111/j.1528-1167.2006.00860.x.

[33] Sprengers M, Vonck K, Carrette E, Marson AG, Boon P. Deep brain and cortical stimulation for epilepsy. Cochrane Database Syst Rev 2014. https://doi.org/10.1002/14651858.CD008497.pub2.

[34] Järvenpää S, Peltola J, Rainesalo S, Leinonen E, Lehtimäki K, Järventausta K. Reversible psychiatric adverse effects related to deep brain stimulation of the anterior thalamus in patients with refractory epilepsy. Epilepsy Behav 2018;88: 373–9. https://doi.org/10.1016/j.yebeh.2018.09.006.

[35] Appleby BS, Duggan PS, Regenberg A, Rabins PV. Psychiatric and neuropsychiatric adverse events associated with deep brain stimulation: a meta-analysis of ten years' experience. Mov Disord 2007;22:1722–8. https://doi.org/10.1002/mds.21551.