



Personality changes in patients suffering from drug-resistant epilepsy after surgical treatment: a 1-year follow-up study

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ABSTRACT

Objective: To determine changes in dimensions of personality in a sample of patients suffering from drug-resistant epilepsy at the 1-year follow-up following surgery, compared to non-surgically treated controls.

Methods: We conducted a prospective comparative controlled study, including drug-resistant epilepsy surgery candidates. Demographic, psychiatric, neurological, and psychological data were recorded. Presurgical and 12-months follow-up evaluations were performed. Personality dimensions were measured by the NEO Five-Factor Inventory, Revised version (NEO-FFI-R), anxiety and depression symptoms were assessed by the Hospital Anxiety and Depression Scale (HADS: HADA-Anxiety and HADD-Depression), psychiatric evaluations were performed using the Diagnostic and Statistical Manual of Mental Disorders, fourth edition (DSM-IV) Axis-I disorders classification. Statistical analysis consisted of comparative tests, correlation analysis, and the stepwise multiple regression test (ANOVA).

Results: A 1-year follow-up was completed by 70 out of 80 patients. Through the study, the surgical group decreased in neuroticism and increased in agreeableness. The controls increased in conscientiousness, and these changes were predicted by the earlier age of epilepsy onset and lesser score in HADD at the baseline. No personality changes were associated with seizure frequency. The presurgical evaluation concluded that both groups had no differences in demographic, psychiatric, or neurological variables with the only exception being for the number of seizures per month, which was higher in the surgical group. Psychiatric comorbidity in patients was associated with their higher degree of neuroticism and agreeableness at the baseline.

Comparing control and surgical groups at the one-year follow-up, the agreeableness personality variable was higher in the surgical group, and as expected, HADS scores were higher in the control group, and seizure frequency was also higher in the control group.

Significance: Higher agreeableness was the most relevant difference in personality dimensions in patients who underwent surgical treatment compared with the non-surgical treatment group. After surgery patients decreased in neuroticism and increased in agreeableness scores.

1. Introduction

Epilepsy is a common neurological disorder affecting more than 50 million people all over the world (Ngugi et al., 2011). There are about 30

% of patients with epilepsy who do not have an adequate response to antiepileptic pharmacotherapy (Kwan and Brodie, 2000). Drug-resistant (or refractory) epilepsy is defined when attempts to choose an appropriate drug treatment are unsuccessful after two different antiepileptic

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drug therapies and uncontrolled seizures continue (Kwan et al., 2010).

Drug-resistant epilepsy is associated with a high burden on health care, patients' low index of quality of life, and high comorbidity, especially with psychiatric diseases (Janson and Bainbridge, 2021; Hitiris et al., 2007). Surgery is the treatment of choice in the case of diagnosed drug-resistant epilepsy, and it aims to achieve a seizure-free outcome and improve the quality of a patient's life (Duncan et al., 2006; Wiebe et al., 2002).

It is known that, compared to the general population, epileptic patients can exhibit specific features of personality; for instance, a high level of aggression (Shehata and Bateh, 2009) and dysfunctional personality patterns (Novais et al., 2019; Bear and Fedio, 1977). As for non-pathological personality dimensions, epileptic patients can show a high level of neuroticism (Rivera Bonet et al., 2019) and a low level of openness to experience (Leong et al., 2019), compared to the general population.

After analyzing personality changes in patients with drug-resistant epilepsy following successful surgical treatment, the decrease in the expression of pathological personality traits and the reductions of subscales of neuroticism and organic psycho-syndrome were reported (Novais et al., 2019; Witt et al., 2008). Such pathological personality patterns such as social introversion, paranoia, psychasthenia, hypochondriasis, and schizophrenia significantly decreased following surgical treatment in patients suffering from drug-resistant epilepsy in observational follow-up studies using the *Minnesota Multiphasic Personality Inventory* (MMPI) (Meldolesi et al., 2007; Derry et al., 2002; Wachi et al., 2001; Meier and French, 1965). In contrast, some researchers revealed no personality changes in patients with epilepsy following surgical treatment (Engman and Malmgren, 2012; King and Tranel, 2017).

Epileptic patients show higher neuroticism compared to the general population (Rassart et al., 2020), and some studies focused on this dimension. Some authors reported neuroticism did not change following surgery (Engman and Malmgren, 2012; Rose et al., 1996), but Witt with colleagues (Witt et al., 2008) demonstrated changes in some subscales of this dimension in their research. A recent systematic review (Iurina et al., 2021), studied personality changes in patients with drug-resistant epilepsy following surgical treatment, and came to the conclusion, that some personality dimensions could change following surgery. These changes can differ according to the localization of the epileptogenic area; for example, the insular resection group became more emotionally labile despite seizure freedom, compared to the temporal group who increased in lack of stamina scale (Hébert-Seropian et al., 2017).

Seizure freedom as an outcome of surgical treatment can influence the existence of adaptive personality changes and their severity. Favourable personality changes can be seen from early follow-up assessments even in patients who were not seizure-free, though further follow-ups showed that improvements after 1–2 years were specific to seizure-free patients. Taking into account that pathological personality features are the result of a continuing interictal process and brain structure damage caused by epileptic activity or side effects of antiepileptic treatment (Hessen et al., 2007), it is expected that achieving seizure freedom may lead to changes in the severity of these personality traits in patients and recovery from several psychiatric symptoms. Reviewing current literature revealed a lack of studies to analyse changes in non-pathological personality features following surgery in drug-resistant epilepsy. The present study aimed to evaluate the changes in dimensions of personality using the NEO-FFI-R questionnaire in drug-resistant epilepsy patients who underwent surgical treatment, compared to a control group in one-year follow-up.

2. Methods

2.1. Design

We carried out an observational, prospective cohort study, in which

a study group of drug-resistant epileptic patients, who underwent surgical treatment, was compared with a control group consisting of patients suffering from drug-resistant epilepsy treated with antiepileptic drugs. Both groups were followed up to 1 year after being included in the study.

2.2. Setting and participants

This research was conducted at the Hospital Clinic of Barcelona. The study was approved by the Hospital Ethics Committee. Subjects were recruited from the Epilepsy Unit of the Neurology Service, which receives referrals from the whole of Spain.

The general evaluation protocol consisted of the following points: all participants signed informed consent; the patients were evaluated to confirm the diagnosis of drug-resistant epilepsy according to the International League Against Epilepsy protocol (Scheffer et al., 2017) and were assessed for the possibility of surgical intervention. Patients with one or more of the clinical conditions listed below were excluded from the current study:

- 1) history of serious medical pathology except for epilepsy;
- 2) mental retardation: IQ < 70;
- 3) presence of severe dementia previously diagnosed;
- 4) schizophrenia or other chronic psychosis;
- 5) non-epileptic psychogenic seizures;
- 6) surgical intervention for control of previous epileptic seizures.

Those, who met the inclusion criteria of the study, but had contraindications for surgery according to the Epilepsy Committee report, constituted the control group.

2.3. Clinical assessments

Demographic, clinical, psychiatric, and psychological variables were collected. Demographic data collection form included age, gender, education, occupation, and marital state. Clinical data consisted of information about the age of the epilepsy onset in months, etiology of epilepsy, localization, and laterization of epileptogenic foci, type of epileptic seizures, dichotomic measure of a number of seizures at the baseline ("5 or less per month" or "more than 5 per month"), and a number of seizures per month in the last 6 months. Psychiatric evaluations were performed by a psychiatrist, and they included DSM-IV Axis-I disorders and HADS – depression and anxiety scale. Evaluation of personality dimensions was performed by using NEO-FFI-R (Aluja et al., 2005). The revised NEO-FFI (NEO Five-Factor Inventory) is a short version of the NEO-PI-R (Revised NEO Personality Inventory) questionnaire and has 60 items (12 per domain) for self-assessing the five major personality dimensions: neuroticism, extraversion, openness to experience, agreeableness, and conscientiousness.

The patient must indicate his/her degree of agreement with the statement using a score from 0 to 4 from "total disagreement" to «totally agree» respectively. The minimum score for any domain is 0, and the maximum is 48. The average scores of each variable in the Spanish population are: Neuroticism: Mean = 23.48, SD = 9.04; Extraversion: Mean = 29.73, SD = 7.50; Openness to experience: Mean = 30.66, SD = 7.22; Agreeableness: Mean = 36.15, SD = 6.63; Conscientiousness: Mean = 33.38, SD = 7.66. Neuroticism is a disposition to experience negative effects, such as anger, irritability, emotional instability, anxiety, and depression. Extraversion is characterized by sociability, assertiveness, high activity level, positive emotions, and in search of stimulation. Openness trait involves being creative, curious, interested in new experiences and being emotionally and artistically sensitive. Agreeableness is the domain of emphatic emotion, expressing the ability to help and cooperate for the well-being of society. Conscientiousness reflects the tendency to be responsible, strong willed, persistent, organized, goal-directed, and adherence to rules and ethical principles.

Anxiety and depressive symptoms were assessed by Hospital Anxiety and Depression Scale (HADS). The Spanish version of HADS was applied for evaluating depression (HAD - D) and anxiety (HAD - A) (Herrero et al., 2003). It contains 14 items, 7 of which are for self-assessing the level of depression and 7 for anxiety. Every subscale should be scored by the patient from 0 to 3 according to the severity of the item. Accordingly, the patient can score from 0 to 21 points on each scale. More than 10 points out of 21 in every subscale is considered as a probable indicator of clinical anxiety or depression.

The clinician version of the Structured Clinical Interview for DSM-IV (SCID-CV; Spanish version) (First et al., 1996) was used to assess DSM-IV Axis-I disorders. We grouped psychiatric comorbidity into two clusters: "yes"/"no". The following psychiatric conditions were evaluated: 1) affective disorders, including major depressive episodes, recurrent depression, dysthymic disorder, affective disorder due to a medical condition or substance disorder, adjustment disorder, and bipolar disorder; 2) anxiety disorders, including panic disorder, phobia, obsessive-compulsive disorder, posttraumatic stress disorder, and other anxiety disorders; 3) schizophrenia or schizoaffective disorder and other psychosis; 4) eating disorders; 5) conduct disorder; and 6) substance use disorder.

2.4. Procedure

All participants provided written informed consent at the time of their enrollment in the outpatient setting of the Epilepsy Unit. Drug-resistant epilepsy was diagnosed according to the International League Against Epilepsy protocol. Accepted patients were referred for admission to a neurology ward for a week evaluation.

Clinical evaluation included video-electroencephalography (EEG) monitoring, a 3 - Tesla brain magnetic resonance with an epilepsy protocol, functional magnetic resonance imaging (fMRI), positron emission tomography scans to indicate the epileptogenic zone, neuropsychological tests, the psychiatric evaluation, and a psychological evaluation through the NEO-FFI-R. Taking all these results into account the committee board made a decision on the surgery suitability for every patient. The epilepsy committee comprises neurologists, psychiatrists, neurosurgeons, neuroradiologists, neuropsychologists, psychologists, and nuclear medicine specialists.

Those who had contraindications for surgical intervention formed the control cohort. Surgical candidates were paired with the same time following patients, who composed the control group and underwent all assessment procedures at the same time interval respectively to the surgical intervention at the baseline and in 1 year after surgery. Non-surgical patients were maintained on a standard medication regimen during the follow-up period. The postoperative evaluation 1-year following surgical treatment involved the following procedures: the psychiatric evaluation (HADS), the clinical psychology assessment (NEO-FFI-R), and a clinical interview to collect neurological data.

2.5. Statistical analysis

Statistical analysis was performed using Version 22 of SPSS for Windows and differences were considered significant at $p < 0.05$.

Distributions of variables were examined by Shapiro-Wilk Test according to our sample size and appropriate tests were applied for further analysis.

The intention to treat approach was carried out in order to see if the 10 drop-out patients were different from patients finishing the follow-up. A descriptive analysis of all variables was performed at the baseline. The group of controls and the surgical group were compared to detect initial differences between groups, using a Student's *t*-test, Pearson's chi-square test, Mann-Whitney *U* test according to the type of every variable and its distributions. When a difference was found, how it affected personality was examined using Kruskal-Wallis tests and Student's *t*-test. Also, stepwise multiple regression (ANOVA), Student's *t*-

test, and Spearman correlation analysis was run for all the independent variables to reveal how they are initially associated with the personality profile. The independent variables included age, gender, type of epilepsy, location, laterality, etiology, age at epilepsy onset, HADS, and mental disorders (existence or absence: yes/no). To evaluate changes in psychological and psychiatric test results from baseline to 1-year follow-up, Student's *t*-test, within-subjects Wilcoxon signed-rank test, and Spearman correlation tests were performed. Adjustments for multiple tests were performed using the Games-Howell procedure.

Those variables of personality test that reached statistical significance in 1-year follow-up were introduced into stepwise multiple regression analysis. Multiple regression was used to determine the contribution of each variable at the baseline on the changes in personality dimensions at the 1-year follow-up. Also, such data as seizure frequency at the baseline, seizure frequency at the 1-year follow-up, and the variable reflecting changes in this item in pre/post follow-up period were included in the Spearman correlation tests to be compared with variables indicating changes in personality dimensions.

3. Results

Of 80 eligible patients, 70 completed the neuropsychiatric assessment at the 1-year follow-up, 28 underwent surgery, and 42 were not suitable for surgery (control group). In the intention to treat approach, no statistical differences in sociodemographic, clinical, or neuropsychiatric variables were revealed between patients who completed the study and patients who were lost to 1-year follow-up ($n = 10$).

3.1. Descriptive analysis at baseline and comparison between groups

Sociodemographic, clinical, and neuropsychiatric variables at the baseline in the whole sample and the differences between groups are shown in Table 1.

Given that we found the baseline differences in the number of seizures at the basal time (per month), we analyzed this variable affection on the personality dimensions. Thus, in Table 2, we compared personality dimensions according to the basal seizure frequency dichotomized, and no differences between both groups were observed. Tables 3A and 3B presents the analysis of how personality dimensions were associated with all the independent sociodemographic and clinical variables at the baseline.

3.2. Longitudinal analysis of one-year follow-up outcomes

Table 4 shows longitudinal changes in personality, mood, and seizure frequency in the surgical and non-operated group through the study, as well as differences between groups at the one-year follow-up. Significant differences between basal and 1-year meanings in the surgical group were observed in decreased neuroticism (Mean = 4.46, SD = 6.05, $p = 0.001^*$), and increased agreeableness scores (Mean = -2.16, SD = 4.20, $p = 0.011^*$). Conscientiousness increased in the control group through the 1-year follow-up: Mean = -2.36, SD = 4.71, $p = 0.002^*$.

The comparison of control and surgical groups revealed the only significant difference in agreeableness personality variable, being higher in the operated group ($p = 0.007^*$).

The number of seizures diminished significantly in the surgical group only (Mean = 26.04, SD = 37.52, $p = 0.000^{**}$). Differences were observed in the number of seizures per month comparing both groups of patients at the one-year follow-up, with higher scores in the controls: $z = -5.394$, $p = 0.000^{**}$.

We evaluated how the variable, reflected personality changes from the baseline to the 1-year after surgery, depended on the number of seizures at the one-year follow-up and pre-post differences in seizures frequency: no statistically significant associations with these variables were observed either in the surgical group or the control group.

Table 5 demonstrates changes in mood and differences between

Table 1
Sociodemographic and clinical variables at baseline and differences between groups.

	Whole sample group			Surgical group			Control group			Differences between surgical and control group, p-value
	(n = 70)			(n = 28)			(n = 42)			
	%	Mean	SD	%	Mean	SD	%	Mean	SD	
Sociodemographic										
Age		36.94	10.93		35.00	8.49		38.24	12.22	0.195
Gender:										0.728
Women	55.7			53.6			57.1			
Men	44.3			46.4			42.9			
Education:										0.768
Basic education	45.7			46.4			45.2			
Secondary education	37.1			39.3			35.7			
Higher education	17.1			14.3			19			
Occupation:										0.073
Inactive	28.6			14.3			38.1			
Housewife/student	21.4			21.4			21.4			
Active	50			64.3			40.5			
Marital status:										0.519
Married	57.1			64.3			52.4			
Separated/widowers	12.9			7.1			16.7			
Single	28.6			28.6			28.6			
No data	1.4			0			2.4			
Neurologic										
Idiopathic etiology	60.0			64.3			57.1			0.819
Type of seizures:										0.599
No seizures	1.4			0			2.4			
Focal onset impaired awareness seizures	50.0			57.1			45.2			
Other focal onset seizures	15.7			14.3			16.7			
Unknown onset tonic-clonic seizures	20			14.3			23.8			
Generalized seizures	10.0			14.3			7.1			
Locus:										0.571
Temporal	57.1			64.3			52.4			
Extratemporal	24.3			25.0			23.8			
Unestablished	15.7			10.7			19			
Hemisphere:										0.400
Right	44.3			42.9			45.2			
Left	37.1			46.4			31			
Bilateral	12.9			7.1			16.7			
Unknown	1.4			0			2.4			
Age (months) of epilepsy onset		193.6	180.34		139.57	120.77		229.62	204.46	0.068
Number of seizures at the basal time (per month)		21.11	35.71		26.04	37.52		17.83	34.52	0.040*
Psychiatric assessment:										
Psychiatric comorbidity	37.1			50			12			
HADS scale:										
HAD-Depression		3.93	3.41		4.59	4.09		3.49	2.86	0.308
HAD-Anxiety		6.59	3.52		7.16	3.87		6.18	3.21	0.203
Clinical psychology assessment										
NEO personality:										
Neuroticism		25.53	6.85		26.66	6.90		24.78	6.77	0.254
Extraversion		26.61	5.90		25.87	6.30		27.10	5.65	0.395
Openness to experience		27.55	6.27		27.46	6.51		27.60	6.19	0.923
Agreeableness		32.73	5.07		33.82	5.36		32.00	4.79	0.141
Conscientiousness		32.48	5.90		33.45	6.95		31.84	5.86	0.265

HADS scoring for each variable: Normal: 0–7; Borderline abnormal (borderline case): 8–10; Abnormal (case): 11–21.

The average scores of each NEO-FFI-R variable in the Spanish population are: Neuroticism: Mean = 23.48, SD = 9.04; Extraversion: Mean = 29.73, SD = 7.50; Openness to experience: Mean = 30.66, SD = 7.22; Agreeableness: Mean = 36.15, SD = 6.63; Conscientiousness: Mean = 33.38, SD = 7.66.

surgical and control groups at the 1-year follow-up. HADA and HADD scores were higher in the control group, comparing to the surgical group at the 1-year follow-up ($p = 0.044^*$ and $p = 0.018^*$ relatively for anxiety and depression scores). The number of seizures diminished significantly in the surgical group only (Mean = 26.04, SD = 37.52, $p = 0.000^{**}$). Differences were observed in the number of seizures per month comparing both groups of patients at the one-year follow-up, with higher scores in the controls: $z = -5.394$, $p = 0.000^{**}$.

We evaluated how the variable, reflected personality changes from the baseline to the 1-year after surgery, depended on the number of

seizures at the one-year follow-up and pre-post differences in seizures frequency: no statistically significant associations with these variables were observed either in the surgical group or the control group.

3.3. Predictive analysis from baseline variables to one-year follow-up outcomes

The surgical group increased in neuroticism and agreeableness, which was not predicted by any baseline variables of interest.

The controls increased in conscientiousness; these changes were

Table 2
Association of NEO-FFI personality dimensions and seizure frequency (intervals) at the baseline (presurgical evaluation) in a 70 drug-resistant epilepsy patients' sample.

	Seizure frequency	N of patients	Mean	SD	Differences between groups, p-value
Neuroticism	5 or less per month	30	24.94	6.87	p = 0.532
	More than 5 per month	40	25.98	6.88	
Extraversion	5 or less per month	30	26.99	4.68	p = 0.634
	More than 5 per month	40	26.33	6.72	
Openness to experience	5 or less per month	30	26.37	6.36	p = 0.174
	More than 5 per month	40	28.43	6.14	
Agreeableness	5 or less per month	30	32.59	4.35	p = 0.846
	More than 5 per month	40	32.83	5.59	
Conscientiousness	5 or less per month	30	32.93	5.82	p = 0.589
	More than 5 per month	40	31.15	6.02	

Personality was not associated with the seizure frequency in our sample.

predicted by the earlier age of epilepsy onset and lower depression scores at the baseline ($R^2 = 27.8\%$, $p = 0.002$, $\beta = -0.363$ and -0.302 respectively). Also, the controls increased in HADS scores, which was not predicted by any baseline variables of interest.

4. Discussion

It was revealed that personality traits in patients with drug-resistant epilepsy change following surgical and pharmacological antiepileptic treatment at the 1-year follow-up, but in a different way depending on whether or not surgical treatment is carried out. This is the most important outcome of our study. These personality changes were not

Table 3A

Association of personality dimensions with neurological and sociodemographic variables at the baseline (presurgical evaluation) in a 70 drug-resistant epilepsy patients' sample.

	Age	Gender	Etiology	Type of the seizures	Locus	Hemisphere (right vs left vs bilateral)	Age (month) of epilepsy onset	Number of seizures at basal time (per month)
Neuroticism	Pearson Correlation = 0.040p = 0.743	F = 0.530t = 1.109df = 68p = 0.271	F = 0.108t = 0.369df = 65p = 0.694	F = 1.535p = 0.214	F = 0.310p = 0.735	F = 0.366p = 0.695	Correlation coefficient = 0.238p = 0.047*	Correlation coefficient = 0.074p = 0.543
Extraversion	Pearson Correlation = 0.218p = 0.070	F = 1.753t = 1.413df = 68p = 0.162	F = 0.064t = 0.800df = 65p = 0.925	F = 0.745p = 0.529	F = 0.282p = 0.755	F = 0.346p = 0.709	Correlation coefficient = 0.273p = 0.022*	Correlation coefficient = 0.038p = 0.755
Openness to experience	Pearson Correlation = 0.014p = 0.907	F = 0.000t = 0.806df = 68p = 0.423	F = 0.025t = 1.017df = 65p = 0.313	F = 0.833p = 0.480	F = 2.114p = 0.129	F = 0.504p = 0.606	Correlation coefficient = 0.102p = 0.401	Correlation coefficient = 0.139p = 0.252
Agreeableness	Pearson Correlation = 0.106p = 0.382	F = 0.256t = 2.383df = 68p = 0.020* (W > M)	F = 0.003t = 1.467df = 65p = 0.313	F = 0.263p = 0.852	F = 0.407p = 0.668	F = 3.898p = 0.025* (R > L > B)	Correlation coefficient = -0.59p = 0.626	Correlation coefficient = 0.146p = 0.228
Conscientiousness	Pearson Correlation = 0.189p = 0.117	F = 0.356t = 3.512df = 68p = 0.001** (W > M)	F = 0.029t = 0.535df = 65p = 0.595	F = 0.819p = 0.488	F = 0.835p = 0.439	F = 0.880p = 0.420	Correlation coefficient = 0.029p = 0.810	Correlation coefficient = 0.039p = 0.750

W: women; M: men; R: right; L: left; B: bilateral.

Age of the epilepsy onset, hemisphere of the epileptogenic focus, and gender were associated with personality in our sample.

* p < 0,05.

** p < 0.001.

associated with seizure status. The most relevant features in our study were a decrease in neuroticism and an increase in agreeableness in the surgical group through the follow-up, and higher agreeableness in the surgical group compared with the control group one year after surgery.

Decrease in neuroticism one year after surgical treatment in epileptic patients was presented in another study (Witt et al., 2008) with 151 epileptic patients, with a mean age of 37.1 years. However, the German personality inventory was used for personality assessment in this case instead of being performed with the NEO-FFI-R as we did. The German personality inventory (*Fragebogen zur Persönlichkeit bei zerebralen Erkrankungen*) aims to identify behavioral and personality patterns in non-psychiatric patients with central nervous system disorders and epilepsy in particular. The scale of neuroticism corresponds to the identically named trait of the Big Five Personality Inventory, but includes some reflected pathological features subscales: vegetative symptoms, anxiety, somatization, hyperemotionality, reduced drive, obsession, and other-determination. Additionally, they reported on the personality changes in seizure-free patients only. With reference to somatic and psychic anxiety as items of the neuroticism-related scale, another study (Engman and Malmgren, 2012) also found a decrease in these features evaluated by the Karolinska Scale of Personality in 57 epileptic patients, with a mean age of the participants similar to ours, after surgical treatment. These neuroticism-related subscales are quite similar to the NEO - neuroticism item, but these items are part of a wider neuropsychological feature in the Karolinska Scale of Personality - from scales related to neuroticism and anxiety proneness. Personality changes were revealed in seizure-free patients only (Engel I). In another study (Rassart et al., 2020) with 53 patients, and a mean age of 30 years the shortened Dutch version of the Big Five Inventory was used to evaluate personality. The Liverpool Seizure Severity Scale was used to assess seizure frequency and severity. The association of a high level of neuroticism and a low level of agreeableness with seizure frequency in epileptic patients was detected in that research. In contrast, in our analysis, we found no association of these personality changes with the number of seizures per month neither pre- nor post changes in seizure frequency variables. Wachi et al. (2001) reported no differences between seizure-free and non-seizure-free groups in personality changes in a small sample of 26 epileptic patients following surgical treatment. But patients from the non-seizure-free group showed a reduction in seizure frequency of up to 90 % from a preoperative level. The authors applied the MMPI questionnaire for personality assessment in their study and reported a decrease in the scores of infrequency, hypochondriasis, psychasthenia,

Table 3B

Association of personality dimensions and mood and psychiatric comorbidity at the baseline (presurgical evaluation) in the sample of 70 drug-resistant epilepsy patients.

	HAD-Depression	HAD-Anxiety	Psychiatric comorbidity (yes/no)
Neuroticism	Correlation coefficient = 0.441 p = 0.000 **	Correlation coefficient = 0.528 p = 0.000 **	F = 0.297, t = -2.444, df = 68, p = 0.017* (Neuroticism is higher in patients with psychiatric comorbidity)
Extraversion	Correlation coefficient = -0.501 p = 0.000 **	Correlation coefficient = -0.080 p = 0.518	F = 4.926, df = 38.674, t = 1.895, p = 0.066
Openness to experience	Correlation coefficient = -0.278 p = 0.022 *	Correlation coefficient = -0.141 p = 0.252	F = 1.202, t = 0.228, df = 68, p = 0.821
Agreeableness	Correlation coefficient = -0.235 p = 0.054	Correlation coefficient = 0.095 p = 0.439	F = 0.801, t = -2.357, df = 68, p = 0.021* (Agreeableness is higher in patients with psychiatric comorbidity)
Conscientiousness	Correlation coefficient = -0.101 p = 0.413	Correlation coefficient = 0.101 p = 0.411	F = 0.031, t = -0.008, df = 68, p = 0.993

Psychiatric comorbidity and mood were associated with personality in our sample.

* p < 0,05.
** p < 0,001.

and schizophrenia in patients following surgical treatment. Thus, the improvement in pathological personality traits can be observed even in the case of reduction in seizure frequency, rather than complete seizure elimination.

These differences between our and other studies may occur due to the different inventories applied to assess personality and seizure

frequency. We did not have a “seizure-free” group in our analysis: we indicated the number of seizures for every patient or 2 groups according to the seizure frequency (“5 or less per month” and “more than 5 per month”) for different statistical calculations.

In our research, the control group increased in consciousness at the one-year follow-up, which was predicted by an earlier age of epilepsy onset and lower depression symptoms measured by HADD at the baseline.

Consciousness is defined as an individual’s organization, persistence, and motivation in achieving a goal (Roberts et al., 2009). Increase in this complex trait of character in a control group appears as an adaptive process and psychologically tackling disease-associated stress, which goes better in more emotionally stable individuals, who are less depressed.

Conscientiousness and agreeableness were significantly higher in women than in men at the baseline in our sample. We cannot completely confirm or deny the idea of personality gender differences in epileptic patients vs the general population, as there are different results reported in the literature. Some general population studies (Chapman et al., 2007; Costa et al., 2001) indicated women being higher in agreeableness and neuroticism scores than men; one research (Weisberg et al., 2011) reported on higher extraversion additionally to the features mentioned above. Nostro et al. (2017) reported that neuroticism and conscientiousness were higher in women than in men in the general population. According to the research of Mac Giolla and Kajonius (2019) women typically score higher than men in all five trait factors in the general population. All the above-mentioned studies reported women being more neurotic than men in the general population. However, this differs from our results which revealed no significant gender differences in the neuroticism scores. It could be due to the fact that epilepsy is associated with increased neuroticism in patients compared with the general population regardless of gender (Rivera Bonet et al., 2019), so epileptic men become more neurotic compared with men without epilepsy.

Agreeableness was lower in the bilateral epileptogenic foci localization subgroup in comparison to the right and left hemispheres. There are no personality differences between the right and left localized epilepsy foci, which is in line with another epileptic patient’s study results

Table 4

Changes in NEO-FFI-R dimensions and seizure frequency at the one-year follow-up in the surgical and control groups of drug-resistant epilepsy patients.

	Surgical group					Control group					Differences between groups, p-value
	Results		Differences (basal-1 year)			Results		Differences (basal-1 year)			
	Mean	SD	Mean	SD	p	Mean	SD	Mean	SD	p	
NEO-FFI-R:											
Neuroticism	22.19	9.50	4.46	6.05	0.001**	23.97	9.05	0.81	7.42	0.484	0.433
Extraversion	27.37	6.62	-1.49	6.83	0.258	27.27	7.08	-0.16	4.72	0.826	0.954
Openness to experience	28.22	8.12	-0.77	5.70	0.484	28.03	6.20	-0.42	5.51	0.624	0.909
Agreeableness	35.98	5.27	-2.16	4.20	0.011*	32.17	5.92	-0.17	5.12	0.828	0.007*
Conscientiousness	35.36	6.18	-1.91	5.53	0.079	34.19	6.60	-2.36	4.71	0.002*	0.460
Seizure frequency	0.96	2.99	26.04	37.52	0.000**	15.56	21.21	2.68	25.54	0.866	0.000**

Personality and seizure frequency changed in both groups of patients at the 1-year follow-up.

* p < 0,05.
** p < 0,001.

Table 5

Changes in HADS at the one-year follow-up in the surgical and control groups of drug-resistant epilepsy patients.

	Surgical group					Control group					Differences between groups, p-value
	Results		Differences (basal-1 year)			Results		Differences (basal-1 year)			
	Mean	SD	Mean	SD	p	Mean	SD	Mean	SD	p	
HADS scale:											
HAD-Depression	3.08	3.24	1.51	3.33	0.146	5.15	3.97	-1.66	4.17	0.015*	0.018*
HAD-Anxiety	5.60	4.42	1.56	4.14	0.072	7.73	4.42	-1.55	3.64	0.010*	0.044*

Control group increased in depression and anxiety levels at the 1-year follow-up.

* p < 0,05.

(Leong et al., 2019). According to the results of two studies with healthy participants, special anatomic areas were associated with high agreeableness: larger areas in the left superior temporal gyrus (Li et al., 2017) or larger regional gray matter volume right orbitofrontal cortex (Kapoianis et al., 2013). Our research did not provide enough data for a detailed discussion on this topic, but it seems that anatomical and functional brain features in epileptic patients, who have bilateral localization of epileptogenic foci, can negatively influence agreeableness.

Neuroticism and agreeableness were higher in patients with psychiatric comorbidities at the baseline in our research. The neuroticism domain presented a positive correlation with psychiatric symptoms in both mesial temporal lobe epilepsy related to hippocampal sclerosis in 100 patients and also in a study with 100 juvenile myoclonic epilepsy patients (Alonso et al., 2019).

Agreeableness dimension scores negatively correlated with psychiatric diseases in studies with non-epileptic participants: in a non-clinical sample of 3147 subjects between 17 and 25 years old, who had a psychotic experience in the past (Shi et al., 2018); in 3785 patients between 21 and 46 years old suffering from addictive disorders (Dash et al., 2019); and in a sample of 6140 patients with borderline personality disorder (Distel et al., 2009). Our patients suffering from drug-resistant epilepsy showed a high level of agreeableness in the subgroup with psychiatric comorbidities, and this result does not correspond to the other non-epileptic studies, which evaluated the association of personality and psychiatric disorders.

The most prevalent psychiatric comorbidity in epileptic patients associated with high neuroticism is mood disorders. Our sample showed that neuroticism was associated with higher HADS scores. The higher the neuroticism is, the more depressive and anxious the patient is; which is in line with many previous studies with both epileptic patients and healthy participants (Rivera Bonet et al., 2019; Lee et al., 2018; Kim et al., 2016; Endermann and Zimmermann, 2009; Wilson et al., 2009). Extraversion and openness to experience personality dimensions were negatively associated with depression scores in our research, which is in line with previous studies with healthy participants (Kim et al., 2016), and with neurologic diseases subjects (Magyar et al., 2017).

Our study shows the association between earlier onset of epilepsy and higher conscientiousness scores. Also, a significant correlation between the neuroticism level and the age of epilepsy onset was revealed, indicating that the later in age epilepsy begins, the higher the neuroticism is. Seizure onset during infancy was associated with lower neuroticism scores in adulthood comparing to the group with adolescent seizure onset in another study (Wilson et al., 2009). It may reflect that these individuals became accustomed to living with the disease from an early age and did not have to adapt to epilepsy limitations. Also, earlier epilepsy onset was associated with an increase in conscientiousness in the control group in the 1-year follow-up, which illustrates more flexible adaptive ability in these patients.

Thus, in our sample, the earlier epilepsy onset predicts more favorable personality development and more flexible adaptive ability, compared to the patients with a later age of the disease manifestation. The findings of the study inform clinical psychologists, psychiatrists, and patients, that some personality features and mood can favorably change following surgical treatment. These improvements can have a positive impact on future psychological functioning in patients.

5. Strengths

Our study is one of the few that were carried out with a control group, while most of the studies to date did not have controls. Personality traits were measured by a standardized and validated tool such as NEO-FFI-R.

6. Limitations

The main limitation of this study occurs due to the small sample size. Due to ethical reasons the distribution for groups of surgical treatment or controls depended on patient suitability and was not randomized, which could cause bias in our sample. Furthermore, one of the limitations of the study was the lack of an instrument which could inform about various pathological personality traits. Only through this assessment (and consequent statistical analysis) could we talk about "normal/pathological" personality traits. There are instruments capable of measuring pathological personality, such as DAPP-BQ or NBI.

7. Conclusion

This study demonstrates that personality traits in patients with drug-resistant epilepsy change following surgery at the 1-year follow-up. Agreeableness was the most relevant difference between the surgical and control group, being higher in the former.

The surgical group became less neurotic and increased in agreeableness scores, while the control group increased in the conscientiousness scale, especially if a patient was young at the onset of epilepsy and was not depressed according to the baseline presurgical evaluation. The changes in personality dimensions were not associated with the seizure frequency, either at the baseline or at the follow-up.

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Declaration of Competing Interest

None of the authors has any conflict of interest to disclose. 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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