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Personality patterns of people with medically refractory epilepsy – Does the epileptogenic zone matter?

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ABSTRACT

Objectives: The aims of this study were to determine the rate of dysfunctional personality patterns before and after epilepsy surgery, their types, and the importance of the epileptogenic zone in a sample of people with refractory epilepsy.
Methods: We conducted an ambispective observational study, including refractory epilepsy surgery candidates. Demographic, psychiatric, and neurological data were recorded. Evaluation of personality was made using the Millon Clinical Multiaxial Inventory-II (MCMI-II). Presurgical predictors of personality patterns were determined using a linear regression model. The proportion of patients with dysfunctional personality patterns, before and after surgery, was compared using the Mcnemar's test. Then a generalized estimating equation model was performed to include predictors of changes in this rate.
Results: One hundred and ninety-nine participants were included. Seventy percent had a dysfunctional personality pattern before surgery. After surgery, this percentage dropped to 58%. The difference was statistically significant after adjusting for potential confounders ($p = 0.013$). The most common types were Cluster C personality patterns. Temporal epileptogenic zone was a significant predictor of higher scores of the Avoidant (Coef. 11.8; Confidence Interval (CI) −0.59 23.7; $p = 0.051$) and Compulsive (Coef. 9.55; CI 2.48 16.6; $p = 0.008$) personality patterns and lower scores of Histrionic (Coef. −11.4; CI −21.2 −1.55; $p = 0.024$) and Antisocial (Coef. −8.4; CI −15.6 −1.25; $p = 0.022$) personality patterns, compared to extratemporal epileptogenic zone.
Conclusion: People with refractory epilepsy have high rates of dysfunctional personality patterns. These patterns differ according to the epileptogenic zone.

1. Introduction

The Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5) defines personality disorder as "an enduring pattern of inner experience and behavior the deviates markedly from the expectations of the individual's culture" [1]. This pattern includes impairments in personality (self and interpersonal) functioning and the presence of pathological personality traits, defined as habitual forms of behavior, thought, and emotion that is relatively stable across time and consistent across situations, in each individual [2]. The DSM-5 defines a set of ten types of personality disorders, each one defined by a typical group of dysfunctional personality characteristics or traits. Personality traits, including pathological traits, such as grandiosity, obsessionality, impulsivity or emotional lability, exhibit much higher rates of stability than personality disorders [3]. Personality disorders are organized into 3 clusters: Cluster A (odd/eccentric), including Paranoid, Schizoid, and Schizotypal personality disorders; Cluster B (dramatic/emotional/erratic), including Antisocial, Borderline, Histrionic, and Narcissistic personality disorders; and Cluster C (anxious/fearful), including Obsessive–Compulsive, Avoidant, and Dependent personality disorders [4].

The high prevalence of dysfunctional personality traits among people with epilepsy was noted many decades ago, and it has been discussed over the years. Kraepelin described certain distinctive personality characteristics in these patients, such as meticulousness, slowness, circumstantiality, lability, irritability, explosiveness, and a particular proneness to religiosity [5]. Between 1973 and 1986, Norman Geschwind wrote substantially about what was later called the "Geschwind syndrome", in people with temporal lobe epilepsy (TLE). It included increased religious interests, hypergraphia, increased aggression, increased moral and philosophical concerns, viscosity, and

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seriousness. He also provided an explanation based on the effect of a lesion stimulating the limbic system [6].

Nowadays, some authors still consider the existence of an "interictal personality" in TLE, historically defined as a seizure-based behavioral condition which includes the traits described by Geschwind, and it is assessed using the Neurobehavioral Inventory (NBI) [7]. However, this entity is still controversial, and it has not been included as a specific type of personality disorder in the standard psychiatric classifications [8,9].

Personality traits and personality disorders have been investigated independently in epilepsy. Recent research has shown that people with epilepsy have certain personality characteristics or traits, such as lower self-consideration and self-esteem [10]. Some personality traits may be associated with epilepsy-related factors, namely, earlier age at onset, longer duration of epileptic history, and higher seizure frequency [11].

Regarding personality disorders, diagnosed according to the DSM or the International Statistical Classification of Diseases and Related Health Problems (ICD), their prevalence ranges between 13 and 35% in people with focal epilepsy (mainly TLE) and from 18 to 42% in surgical candidates or people who have undergone surgery [12]. In comparison, the prevalence of personality disorders in the general population ranges between 4 and 15% [13]. The most prevalent types are not consensual among studies. However, cluster C personality disorders, namely obsessive–compulsive, dependent, and avoidant are commonly cited as the most frequent in samples of people with refractory epilepsy [14–16].

Personality disorders in people with epilepsy have been associated with the adaptation or reaction to psychosocial factors, such as stigmatization, low self-esteem, or social isolation [12] but also to epileptic seizure-related factors including a temporal epileptogenic zone, earlier age at onset, longer duration of the disease, and higher seizure frequency [11].

Moreover, personality disorders may also have an impact on the course of epilepsy, potentially affecting adherence to treatment and interpersonal behavior in medical settings [12]. People with preoperative personality disorders also seem to be less likely to become seizure-free after temporal lobe resection [16].

The association of specific personality patterns to the epileptogenic zone and the role of surgery on the longitudinal course of these patterns have not been clearly established. With this study, we aimed to determine the rate of dysfunctional personality patterns and their types in a sample of people with refractory epilepsy. We also searched for epilepsy-related factors associated with these patterns. Finally, we aimed to evaluate the impact of surgery on the rate of these disorders.

2. Methods

This ambispective cohort study was conducted at the Department of Neurosciences and Mental Health of our Institution, between April 2000 and September 2018. Subjects were recruited from our Refractory Epilepsy Reference Centre and the Epilepsy Surgery Group. The diagnosis of refractory epilepsy was made according to the International League Against Epilepsy [17].

The presurgical evaluation included a video-electroencephalography (EEG) monitoring, a 3-Tesla brain magnetic resonance with an epilepsy protocol, functional magnetic resonance imaging (fMRI), and positron emission tomography scans to determine the epileptogenic zone, a neuropsychological, and a psychiatric evaluation. People with temporal and extratemporal epileptogenic zones were included.

Demographic (gender, age, employment status, marital status) and clinical data (etiology of epilepsy, the topography of the epileptogenic zone, the age at onset, time to surgery, and Engel Class [18]) after surgery were collected during interviews and from medical and surgical records. Participants were receiving a minimum of two antiepileptic drugs. However, the type and dosages of these drugs was not addressed in this study because there was considerable variability between patients, as it is usual in people with refractory epilepsy.

This study has been performed in accordance with the ethical standards of the 1964 Declaration of Helsinki and its later amendments and was approved by the Ethics Committee of our institution.

2.1. Subjects

Participants older than 18 years, with refractory epilepsy, included as surgery candidates, with at least one year of primary school education were included in the study. Those with other neurological diseases or intellectual disability were excluded from the analysis.

2.2. Psychiatric evaluation

A psychiatric evaluation was performed by an experienced psychiatrist, before surgery, and one year after the procedure. It included a clinical psychiatric history (demographic data, previous psychiatric history, family history, use of substances as well as other relevant data), the determination of a clinical diagnosis of lifetime and current psychiatric disorders, established according to the ICD-10 [19], and the following personality and psychopathological tests:

2.3. The Millon Clinical Multiaxial Inventory-II (MMCI-II)

The MCMI-II is a psychological assessment tool used to evaluate personality patterns and psychopathology in adults. It includes 13 personality scales, 9 clinical syndrome scales [20], and 3 validity scales to assess response styles on the instrument [21]. This self-report questionnaire includes 175, yes or no questions, regarding patterns of emotional, cognitive and behavioral response. It was developed to evaluate personality prototypes that were included in the Diagnostic and Statistical Manual (DSM). However, as this is not a standardized diagnostic instrument based on DSM diagnostic criteria, we opt to use the more conservative term of "personality patterns" to designate the dysfunctional personality types that it evaluates. For each personality type, the patient's raw scores are converted into Base Rate scores. The presence of a personality trait is denoted by a score of 75 to 84, and a score of 85 or above indicates the persistence of a personality pattern. This version has been validated in clinical samples showing good internal consistency [22].

2.4. The Hamilton Anxiety Rating Scale (HARS)

The scale consists of 14 items and measures both psychic and somatic anxieties [23].

It is scored according to the following cut-offs: 17 = mild; 18–24 = mild to moderate; 25–30 = moderate to severe anxiety [23].

2.5. The Hamilton Depression Rating Scale (HDRS)

The version used corresponds to the original 17 items version. It was developed to access the severity of depressive symptoms [24], and the following scores are generally considered: 0–7 = normal; 8–16 = mild; 17–23 = moderate; >24 = severe depression [25].

2.6. Statistical analysis

The statistical analysis was performed using Stata software (version 14.2; StataCorp, Texas, USA). Descriptive statistics were performed to report the analysis of data presented as mean ± standard deviation or median (minimum–maximum).

For the study of the predictors, before surgery, the outcome variables were the types of personality patterns according to the MCMI-II, analyzed as continuous variables. For the purpose of this study, the psychopathological scales of MCMI-II were not integrated into the analysis. Predictors included the side of the epileptogenic zone, as a categorical variable (right, left, or bilateral), the epileptogenic zone lobe, analyzed as a binary variable (temporal versus extratemporal). Within people

with a temporal lobe epileptogenic zone, mesial versus neocortical zones were also included, as a binary variable. A linear regression model was used for the analysis.

McNemar's test was first used to compare the proportion of patients with a score above 85 at any personality pattern before and after surgery.

Then, to study the longitudinal changes, according to different predictors and potential confounders, a generalized estimating equation model was used including the following variables: type of surgery and Engel class, as binary variables; HDRS and HARS scores, obtained at the one-year evaluation, as continuous variables.

Measures of association were expressed as Coefficients or Odds-Ratio (OR) and a p-value ≤ 0.05 was considered statistically significant.

3. Results

3.1. Demographic and clinical findings

One hundred and ninety-nine participants were included in the sample. Their demographic and clinical characteristics are illustrated in Table 1.

3.2. Psychiatric disorders and personality patterns

At the presurgical evaluation, 33 patients had a current psychiatric diagnosis. Thirty had Major Depression, 1 had a Generalized Anxiety Disorder and another had an Obsessive Compulsive Disorder.

One hundred patients (70%) had a score above the threshold of 85 in at least one personality pattern, in the presurgical evaluation. Regarding their types, most patients (34%) scored above the defined cutoff on more than one pattern. Twenty-three patients scored above the cutoff in 2 types of personality patterns and 26 patients on 3 or more. Most commonly, these patterns corresponded to a mixture of personality types from Cluster C (35%). The second most frequent pattern was the Obsessive–Compulsive (15%) followed by the dependent personality pattern (9%).

3.3. Predictors of dysfunctional personality patterns before surgery

Temporal epileptogenic zone was a significant predictor of higher scores of the Avoidant (Coef. 11.8; CI −0.59 23.7; p = 0.051) and Compulsive (Coef. 9.55; CI 2.48 16.6; p = 0.008) personality patterns and lower scores of Histrionic (Coef. −11.4; CI −21.2 −1.55; p = 0.024) and Antisocial (Coef. −8.4; CI −15.6 −1.25; p = 0.022) personality patterns.

The side of the epileptogenic zone was not found to be a significant predictor of personality. Within people with a temporal epileptogenic zone, mesial and nonmesial locations were also not significantly associated with personality patterns.

3.4. Longitudinal changes in the proportion of patients with pathological personality patterns

After surgery, the percentage of people scoring above 85 dropped to 58%. The difference was marginally significant (OR 4.5; CI 0.93–42.8; p = 0.065) in the first analysis. The personality patterns with the most significant score reductions were Histrionic, Narcissistic, Antisocial, Aggressive, and Passive-Aggressive.

The multivariate generalized estimating equation model including all considered variables showed a statistically significant reduction in the proportion of patients with a dysfunctional personality pattern (Coef. −1.83; CI −3.26 −0.39; p = 0.013) across time. None of the variables included were significantly associated with this decrease.

Medium scores and standard deviation of each personality pattern, before and after surgery, were summarized in Table 2.

A graphical representation of the rate of dysfunctional personality patterns, before and after surgery, was illustrated in Fig. 1.

Medium scores and standard deviation of HARS and HDRS, before and after surgery, were summarized in Table 3.

4. Discussion

In our sample, 70% of people with medically refractory epilepsy displayed a dysfunctional personality pattern before surgery. The most common types were Cluster C personality patterns, which is in line with previous studies [14–16].

One year after surgery, there was a statistically significant reduction in the rate of dysfunctional traits, although of small magnitude. We hypothesize that the removal of the epileptogenic zone or/and the reduction of the interictal epileptic activity might have had a beneficial role. There are very few studies regarding the impact of epilepsy surgery on personality disorders and traits. Previous data using the Minnesota Multiphasic Personality Inventory suggested a decrease in some dysfunctional personality traits, namely, interpersonal sensitivity, irritability, social introversion, hypochondriasis, and psychasthenia, after TLE surgery [26,27].

Additionally, this study showed different personality patterns in people with refractory epilepsy. Those with temporal epileptogenic zones had higher scores in DSM cluster C personality patterns – Avoidant and Compulsive and lower scores in cluster B personality patterns – Histrionic and Antisocial. Since the comparison was made between temporal and extratemporal patients, this implies that those with extratemporal epileptogenic zones (mostly frontal lobe epilepsies)

Table 1
Sociodemographical and clinical characteristics of the participants.

Age, years	38.8 ± 11.6
Males, n (%)	85 (42.7)
Education, years	10.1 ± 4.5
Active workers, n (%)	93 (64.6)
Unemployed, n (%)	39 (21.7)
Retired, n (%)	25 (13.9)
Married, n (%)	74 (50.0)
Age at onset, years	15.9 ± 11.3
Duration of epilepsy, years	22.7 ± 13.0
Temporal epileptogenic zone, n (%)	168 (86.6)
• Mesial, n (%)	106 (65)
• Neocortical, n (%)	57 (35)
Extratemporal epileptogenic zone, n (%)	26 (13.4)
• Frontal epileptogenic zone, n (%)	13 (6.7)
• Multilobar epileptogenic zone, n (%)	10 (5.2)
• Occipital epileptogenic zone, n (%)	2 (1.0)
• Parietal epileptogenic zone, n (%)	1 (0.5)
Laterality of the epileptogenic focus	
• Left	97 (50.8)
• Right	84 (44.0)
• Bilateral	10 (5.2)
Number of antiepileptic drugs	2.3 (0.6)

Table 2
Clinical personality patterns according to MCMI-II.

	Before surgery	One year after surgery
Schizoid	63.2 ± 20.3	67.7 ± 21.5
Avoidant	65.4 ± 25.7	69.9 ± 25.8
Dependent	69.8 ± 24.8	69.9 ± 21.9
Histrionic	61.2 ± 21.3	54.8 ± 23.2
Narcissistic	65.0 ± 20.4	56.2 ± 26.9
Antisocial	62.4 ± 15.5	56.1 ± 17.0
Aggressive	62.6 ± 20.9	56.2 ± 22.0
Compulsive	75.2 ± 15.3	77.3 ± 11.8
Passive-Aggressive	55.5 ± 31.2	47.4 ± 30.8
Self-Defeating	62.3 ± 25.5	63.6 ± 27.9
Schizotypal	61.2 ± 17.8	60.9 ± 21.2
Borderline	55.3 ± 20.7	54.3 ± 21.3
Paranoid	65.7 ± 16.1	64.5 ± 11.5

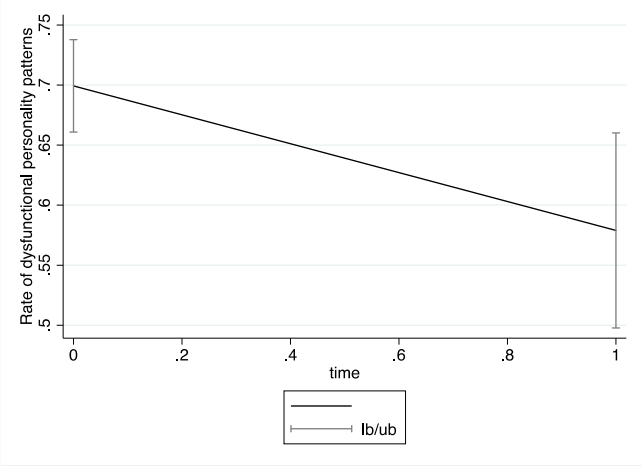

Fig. 1. Dysfunctional personality rates before and one year after surgery.

had higher scores on these cluster B patterns and lower scores on the cluster C patterns.

There is a scarcity of studies focusing on the determination of the neurobiological basis of personality disorders, in people with and without epilepsy. The studies available suggest a link between cluster B personality disorders and frontal lobe dysfunction, while cluster C personality disorders may have an association with temporal lobe dysfunction. In particular, the personality characteristics of "interictal personality" have been associated with mesial epileptogenic zones [6]. More recently, introversion related behaviors and anxiety that may be seen in cluster C personality disorders, have also been associated with mesial temporal pathology [28]. In our work, no differences were detected between patients with mesial versus neocortical temporal epileptogenic zones. This may be due to potential limbic dysfunction even in neocortical epilepsies, to the importance of other temporal zones for social cognition and interaction [29] or to the inability of the test to detect these differences.

Helmstaedter [30] stated that people with TLE tend to manifest more anxiety, neuroticism, and social limitations while those with frontal epilepsy show executive dysfunctions, hyperactivity and addictive behaviors.

Despite the controversy, some of the classical personality characteristics attributed to people with TLE resemble those found in cluster C personality disorders, namely, hypermoralism, dependency, humorlessness, obsessionalism, viscosity, and circumstantiality [31]. On the other hand, people with Juvenile Myoclonic Epilepsy, linked to frontal dysfunction, seem to have more frequent cluster B traits such as impulsive and irresponsible behavior [32]. In a previous study, reversible interictal antisocial behavior was reported in 4 persons with epilepsy involving the prefrontal cortex (OFC). All of these patients fulfilled the DSM-IV criteria for Antisocial Personality disorder and these characteristics remitted following seizure control [33].

Moreover, Pizzi et al. [34], using the Personality Assessment Inventory, reported a similar pattern. In their sample, people with frontal lobe epilepsy had more borderline and antisocial interictal traits than those with a temporal lobe epileptogenic zone. These dysfunctional traits may be related to social cognition deficits, as impaired humor appreciation and decreased ability to detect facial expression [35,36].

A recent study evaluated a patient with crossed obsessive–compulsive personality disorder and impaired theory of mind in TLE. The authors found that this patient revealed impaired interpretation of other people's behavior, mental rigidity, and a tendency to formulate inflexible judgments [37].

The neuroanatomical mechanisms that may contribute to the development of personality disorders have also been investigated in nonepileptic patients. Both the orbital OFC and the anterior cingulate gyrus (ACG) display important roles in social judgment, control of aggression, and other nonsanctioned behavior. Cluster B patients tend to have impairments in these abilities. Disinhibited angry behaviors have been shown both in patients with personality disorders, such as Borderline or Narcissistic and in patients with damage to the prefrontal cortex. This brain area seems to act by inhibiting the amygdala activation, and therefore, inhibiting impulsive aggression [38]. Histrionic personality disorders have been frequently associated with conversion disorders, in particular, psychogenic nonepileptic seizure (PNES) [39]. These disorders also seem to be associated with prefrontal cortex hypoactivation [40]. Raine et al. [41] showed that prefrontal structural deficit, related to a significant reduction in prefrontal gray but not white matter, may underlie the low arousal, poor fear conditioning, lack of conscience, and decision-making deficits that have been found to characterize cluster B personality patterns.

Despite the fact that the neurobiology of Cluster C personality disorders remains mostly unexplored, enlarged striatal and OFC/prefrontal volumes have been shown in patients with obsessive–compulsive traits [4]. We hypothesize that, contrary to cluster B patients, they may have a hypoactivation of the limbic system, both because of excessive inhibition from these cortical areas or dysfunction of important limbic structures such as the amygdala and hippocampus seen in TLE.

This study has some limitations. Firstly, this was an observational study, with a retrospective component, and therefore subject to bias. Different sources of information were considered in order to confirm clinical information and to reduce missing data. Secondly, the MCMI-II corresponds to DSM-III which was the most recent version of this questionnaire when the first surgical candidates were assessed, and we decided to keep it in order to maintain a homogeneous method of personality evaluation. Most of the personality categories and Millon's conception of personality patterns have prevailed until the publication of DSM-5. Despite the fact that MCMI is an important and widely used instrument to evaluate personality, it has never been used in epilepsy, so we cannot compare our results with other studies. Moreover, we also did not apply the NBI and investigated the characteristics of the "interictal personality" syndrome that could be interesting to compare with our MCMI results. Thirdly, the type of antiepileptic drugs was not controlled and these may have an impact on mood and behavior.

Despite these constraints, our study showed some important data regarding personality patterns in people with refractory epilepsy, using a tool designed to evaluate personality prototypes from a standard diagnostic classification system. We showed that most of these patients have a Cluster C Personality Disorder pattern, although different epileptogenic zones may contribute to different dysfunctional personality patterns. Epilepsy surgery may also have a potentially beneficial role on the course of these dysfunctional patterns.

These results may contribute to a better understanding of dysfunctional personality in epilepsy and how epilepsy-related factors may contribute to distinctive dysfunctional patterns. The recognition of the most common personality disorders in epilepsy could improve the management of these patients in the setting of multidisciplinary care. This work may also contribute to the elucidation of the neurobiological basis of personality disorders.

Future studies, with more robust samples, are encouraged to deepen the knowledge of the relationship between epilepsy and personality disorders as well as the potential role of surgery in the long-term course of these psychiatric disorders.

Table 3
HDRS and HARS total scale medium scores.

	Before surgery	One year after surgery
HDRS	8.35 ± 7.8	6.36 ± 6.4
HARS	8.74 ± 7.0	7.06 ± 7.2

Disclosure

The first author is responsible for data collection and integrity.

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None.

Author's contributions

The study design was developed by FN. Patients evaluation was made by LCM, MA, and SL. FN was responsible for data collection and data analysis. FN and AF wrote the manuscript draft. LCM, JP, and LMF reviewed the manuscript draft. All authors have approved the final manuscript.

Declaration of Competing Interest

None.

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