



Personality changes in patients with refractory epilepsy after surgical treatment: A systematic review

Elena Iurina^a, Eva Bailles^b, Luis Pintor^{c,d,*}

^a Department of Psychiatry and Forensic Medicine, Universitat Autònoma de Barcelona, Bellaterra, Barcelona, Catalonia, Spain

^b Clinical Psychologist, Servei de Salut Mental, Hospital Nostra Senyora de Meritxell, Escaldes-Engordany, Andorra

^c Consultation Liaison Psychiatry Unit, Department of Psychiatry and Psychology, Clinical Institute of Neurosciences, Hospital Clínic i Universitari de Barcelona, Universitat de Barcelona, Villarroel, 170, 08036, Barcelona, Catalonia, Spain

^d Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Rosselló, 149, 08036, Barcelona, Catalonia, Spain

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ABSTRACT

Purpose: We aimed to conduct a systematic review to evaluate the personality changes in adult patients with drug-resistant epilepsy following surgical treatment.

Methods: A systematic review was conducted using the Preferred Reporting Items of Systematic Reviews and MetaAnalyses (PRISMA) statement. We searched PubMed, Medline databases, and the Cochrane Controlled Trials Register, with search terms 'personality', 'epilepsy', and 'surgery'.

Results: Eleven studies were selected. In 7 out of 11 studies, personality changes were more adaptive, with patients experiencing decreased neuroticism, impulsivity, hypochondriasis, psychasthenia. One study showed increased emotional lability. The remainder of the studies showed no changes in personality dimensions. Changes in personality differed according to the localization of the epileptogenic area, depended on seizure status after treatment and duration of follow-up. Seizure freedom as an outcome of surgical treatment influenced the existence of personality changes, and their severity. Adaptive personality changes could 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.

Limitations: The main limitation of our research is the heterogeneity of approaches used to evaluate personality in the included studies. Furthermore, the included studies also had different sample sizes and comparison groups, different designs, and different follow-up durations. We only included studies that were written in English.

Conclusions: The majority of studies reported changes in personality dimensions in patients suffering from refractory epilepsy.

1. Introduction

Epilepsy is one of the most serious and common neurological diseases, affecting approximately 50 million people worldwide [1]. Epilepsy is known to be a potentially disabling, chronic, and socially isolating condition, especially in refractory cases. As a severe disease of the central nervous system, it can influence cognitive functions, affecting attention and memory [2,3]. But does epilepsy have an impact on patients' personality? Personality is defined as the characteristic sets of behavior, cognition, and emotional patterns that develop from biological and environmental factors and determine motivation and psychological interactions with one's environment [4,5]. The issue of

personality changes in epilepsy is quite complex and it has been a matter of debate

for decades. According to the current state of the art, personality differences between patients with epilepsy (PWE) and control subjects are usually found to be small and mostly explained by increased anxiety and depression [6–8]. Some authors also indicate higher levels of neuroticism [8,9] and aggression [10] in PWE compared to the general population. Not only the state of disease in general but also the localization of the epileptogenic foci can play a role in the specificity of neuropsychiatric disruptions [11,12]. Temporal lobe epilepsy (TLE) can be linked with increased neuroticism, anxiety, and social limitations compared to patients with frontal epilepsy who demonstrate

* Corresponding author at: Consultation Liaison Psychiatry Unit, Department of Psychiatry and Psychology, Clinical Institute of Neurosciences, Hospital Clínic i Universitari de Barcelona, Universitat de Barcelona, Villarroel, 170, 08036, Barcelona, Catalonia, Spain.

E-mail address: LPINTOR@clinic.cat (L. Pintor).

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hyperactivity, executive dysfunctions, and addictive behaviors [13].

PWE also have lower scores in the Big Five Personality domain "openness to experience" compared to individuals suffering from non-epileptic seizures, and healthy controls [14]. Thus, we do not observe major personality reorganization in patients due to refractory epilepsy, but changes in some domains of personality, mainly in mood.

Previous studies have demonstrated that epilepsy has an influence on some personality domains. We assume that surgery changes the state of the disease in terms of neurophysiological functioning in patients, and,

therefore can also affect their personality.

The current systematic review of studies measuring personality dimensions before and after ST in patients suffering from refractory epilepsy (RE) aims to clarify the question of how changing the state of disease by ST could have an impact on personality in these patients.

2. Materials and methods

The review was performed according to the recommendations of the

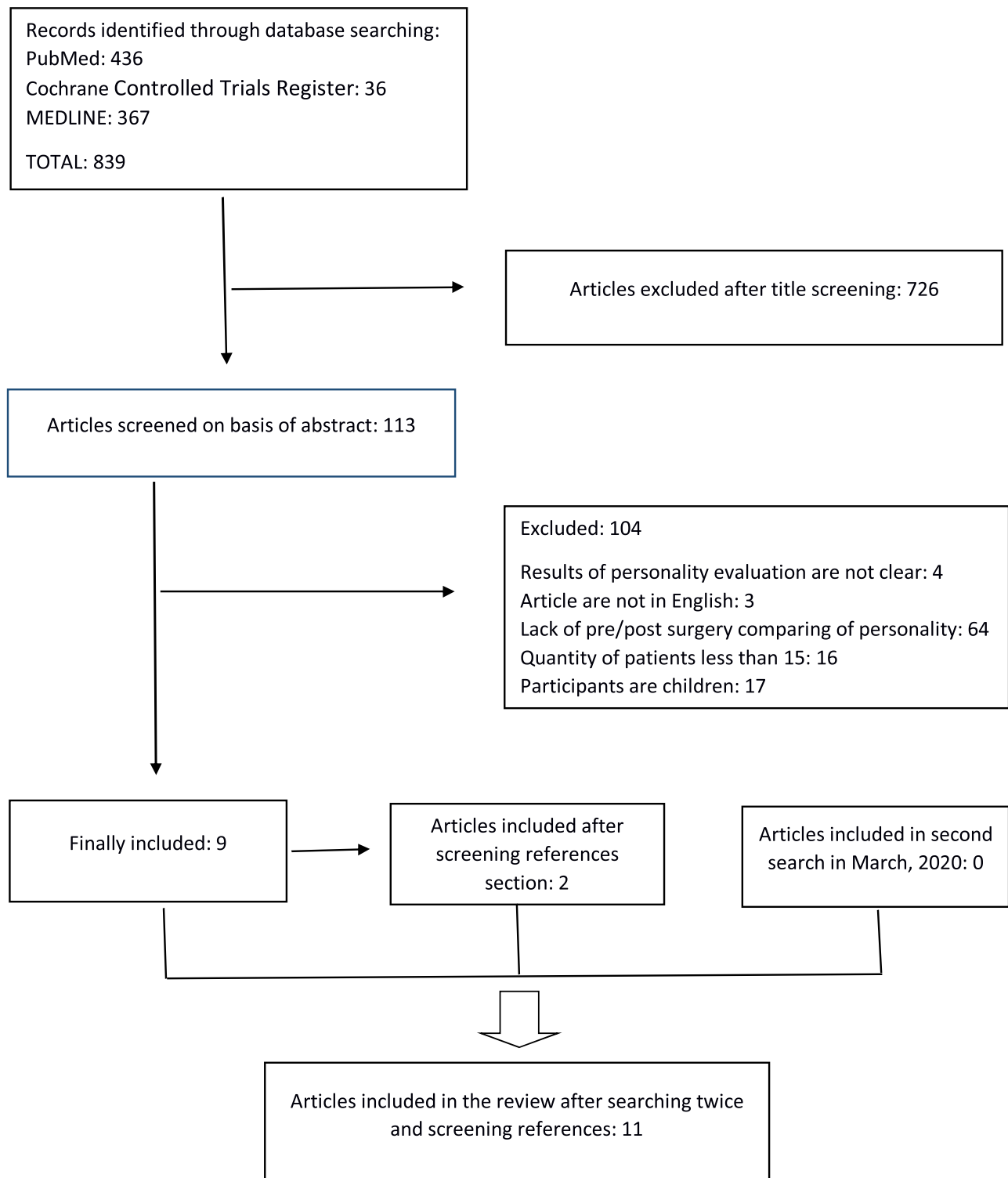


Fig. 1. Chart of studies selected.

Preferred Reporting Items of Systematic Reviews and MetaAnalyses (PRISMA) statement [15].

We conducted this study according to the protocol registered in advance on PROSPERO with ID: CRD42020208243.

2.1. Data sources and search strategy

A literature search was performed using electronic databases such as PubMed, Medline, and the Cochrane Controlled Trials Register. The keywords used were personality, epilepsy, and surgery. The first search was done in November 2019, and the last search was performed in March 2020. The literature search, screening of abstracts, and selection of included trials was performed independently by two investigators (Iurina E., Pintor L.).

2.2. Study selection

We included studies which evaluated personality changes after ST for RE in adults. Only studies written in English were included. The minimum required quantity of patients in a study was 15 participants in order to take into account only original articles with statistical methodology, and avoid to introduce case reports or small series of cases. We included only observational longitudinal follow-up studies, which were case control studies or cohort studies, both prospective and retrospective. Only studies using personality questionnaires were selected, with a follow-up period greater than 6 months. No other limits were set in the study design.

2.3. Data extraction

The data extracted from eligible studies included: the number of participants, in the case of the presence of a control group reasons for comparing were indicated (localization of epileptogenic foci to be resected, seizure outcome postoperatively, and surgical vs non-surgical groups), duration of follow-up period, personality test and particular scales used, and the difference in scores on the personality measure following ST.

3. Results

Initially, 436 publications were identified in Pubmed, 367 in Medline and 36 studies were found in Cochrane Controlled Trials Register. After reviewing the titles, abstracts and removing duplicates, nine studies remained. The references in the studies included from the first round were also reviewed, and two papers were added. Therefore, a total of 11 studies were identified for inclusion in this review. The flowchart shown in Fig. 1 details this process.

A summary of the selected studies is shown in Table 1. In 7 out of 11 studies, after surgery the epileptic patients showed more adaptive personality traits, a decrease in scales of neuroticism, impulsivity, hypochondriasis, paranoidism or increase in control scales. One study showed less appropriate management of emotions. The remaining 3 out of 11 studies showed no changes in personality measures.

8 out of 11 the studies had a comparative group; four studies compared changes in personality according to the localization of epileptogenic area, three studies compared seizure-free (SF) and non seizure-free (NSF) patients, and one study compared surgical and non-operated groups. The sample sizes varied from 24 to 194 participants. The postsurgical follow-up duration ranged from 6 to 24 months. Seven studies applied *The Minnesota Multiphasic Personality Inventory (MMPI)* [16,17], two studies administered *The Iowa Scales of Personality Change* [18], and each of the following measures was used by one study: *The Karolinska scale of personality* [19], *The German personality inventory* [20], and *The Millon Clinical Multiaxial Inventory-II* [21]. *Caudality* was included as an additional scale in one of the studies reviewed, which differentiates frontal from more posterior lesions by MMPI features [22].

Following subsections describe postsurgical personality changes in PWE between groups according to reasons for compare in studies reviewed.

3.1. Influence of localization of epileptic foci to be resected on postsurgical personality changes

One study compared an insular resection group with a TLE cohort [26]. The insular resection group increased in scales of irritability, frugality, anxiety and emotional lability. The TLE group worsened in the “lack of stamina” scale. Another study compared TLE and frontal lobe epilepsy groups, and personality traits remained stable following surgery in both groups [23].

Witt et al. [27] investigated TLE and extra-TLE groups and compared them based on the lateralization of epileptogenic area. There were no deviant differences in these scores, neither pre- nor postoperatively in patients compared with estimated healthy population means. Differences were observed between the subgroups of patients with left and right TLE. The SF left TLE group showed enhanced emotional stabilization, and neuroticism subscale hyperemotionality was decreased, whereas the SF right temporal group showed significantly lower scores in neuroticism items, anxiety and vegetative symptoms postoperatively. The SF right group also showed a decrease in impulsivity – a subscale of organic psycho-syndrome. Meier et al. [28] reported on the improvement in schizoadaptive behavior implications: the right TLE group showed reductions in schizophrenia scale scores, while the left TLE group demonstrated reduced in paranoia and social introversion. Only paranoia item scores changed from being within the clinically significant level to the normal range. Another study comparing TLE and extra-TLE personality changes [8] evaluated the proportion of patients with persistence of any dysfunctional personality pattern pre- and post-surgery. After ST, the proportion of patients with poorly adjusted personality patterns (score above 85 on *The Millon Clinical Multiaxial Inventory-2*) decreased from 70 % to 58 %. The personality patterns with the most significant score reductions were histrionic, narcissistic, anti-social, aggressive, and passive-aggressive. Neither the epileptogenic zone localization nor the lateralization was associated with this decrease.

3.2. Influence of seizure freedom as a surgical outcome on changes in personality

The SF group compare to the NSF decreased in subscales of organic psycho-syndrome and neuroticism following ST in the study of Witt et al. [27]. Another study [29] found a significant decrease in hypochondriasis in the SF group. Changes were seen in the frames of the normal (not deviant) interval of the scores mentioned. Wachi and colleagues in their research [30] concluded that all participants showed decreased scores for infrequency, psychasthenia, hypochondriasis, and schizophrenia in 1 year after ST, without significant differences between the SF and NSF groups. In the study of Wheelock et al. [31] scales depression and psychasthenia were assessed in two postsurgical evaluations: at 2-months and 1-year follow-ups. All patients showed increased above average population scores on both scales at the baseline. The SF group showed a gradual decrease in depression and psychasthenia to levels within the normal range for these traits, whereas NSF patients showed improvement within a short follow-up, but returned to the baseline or even worse within 1 year post-surgery.

3.3. Longitudinal changes in 2 times measured studies

Meldolesi et al. [32] compared the MMPI data obtained at 1- and 2-year follow-ups. Changes were seen within average population interval. Decreases on social introversion and paranoia scales were seen at both time points. In scales used to assess truthfulness, the ‘lie’ and ‘defensiveness’ sub-scale scores were increased after surgery, suggesting

Table 1

Summary of method and results of the studies included in the review.

First Author, year of publication, reference	Type of study	Sample	Period of follow-up	Evaluating of personality	Seizure outcome	Changes in personality after surgery
Novais, 2019 [8]	Comparative, loci of epileptic area	N=168, temporal epileptogenic zone N=26, extratemporal epileptogenic zone	1 year	Millon Clinical Multiaxial Inventory-2	N/A	The reduction in the proportion of patients with a dysfunctional personality patterns was observed without association with localization of epileptic area.
Hebert-Seropian, 2017 [26]	Comparative, loci of epileptic area	N=19, insular epilepsy N=19, temporal lobe epilepsy	> 6 months	Iowa Scales of Personality Change	There were no significant differences between groups in seizure outcome by Engel's classification ($p=0.12$). Average (insular group) meaning= 121; SD=0.54	The insular group demonstrated significant increased scores of Irritability, Lability/ Moodiness, Anxiety and Frugality. TLE group showed significant increased scores of Anxiety, Lack of stamina and Vulnerability to pressure. A significantly higher proportion of patients from the TLE group worsened in Lack of stamina in comparison to the insular group.
King, 2017 [24]	No comparative study.	N=27	>6 months	The Iowa Scales of Personality Change; Minnesota Multiphasic Personality Inventory-2	International League Against Epilepsy (ILAE) seizure outcome classification system ratings averaged 1.89 (SD = 1.22).	Personality and behavior characteristics remained stable.
Engman, 2012 [23]	Comparative, loci of epileptic area	N=39, temporal lobe epilepsy N= 11, frontal lobe epilepsy	2 years	Karolinska Scales of Personality	N/A	Personality features remained stable.
Witt, 2008 [27]	Comparative, loci of epileptic area	N = 26, extratemporal lobe epilepsy (right n=11 left =15); N = 125, temporal lobe epilepsy (right n=65, left =60)	1 year	German personality inventory (Fragebogen zur Persönlichkeit bei zerebralen Erkrankungen).	70.2 % of the patients became seizure-free, i.e. they did not have one single seizure nor any aura within the last 12 months.	All patients showed reduction in Organic Psycho-syndrome and Neuroticism scales. Organic Psycho-Syndrome scale.
Meldolesi, 2007 [32]	No comparative study	N=52, temporal lobe epilepsy	1 year and 2 years	Minnesota Multiphasic Personality Inventory	1-year follow-up outcome: 42 (81 %) completely SF (Engel 1a); 5 (10 %) presented not-disabling auras (Engel 1b); 4 (8%) suffered from rare (1–3 per year) disabling seizures (Engel class 2), 1 (2%) - significant improvement in seizure frequency and severity (Engel class 3). Two years after surgery outcome: 43 (83%) -Engel class 1a, 3 (6%) Engel class 1b, and 6 (12%) - Engel class 2.	Patients decreased in the Social Introversion and Paranoia clinical scales scores; and increased in control scales the Lie and Defensiveness in both follow-up evaluations,
Derry, 2002 [29]	Comparative study, outcome of surgery (seizure free or not)	N=12 seizure-free; N=12 not seizure free	2 years	Minnesota Multiphasic Personality Inventory - 2	SF=12 (no auras or simple partial seizures nor any other kind of epileptic symptoms). NSF=12 (seizures per month: M=4.4, SD=3.7)	SF patients decreased in Hypochondriasis scale mean.
Wachi, 2001 [30]	Comparative study, outcome of surgery (seizure free or not)	N=16, seizure-free; N = 10, not seizure free	1 month, 1 year	Minnesota Multiphasic Personality Inventory	SF=16; NSF=10. The SF group included those who did not have any complex partial or grand mal seizures in the year after the surgery. Auras did not exclude patients from the SF group. the seizure frequency was reduced by 90 %. In 2, the seizure frequency decreased by 75–90 %. In 2 patients the seizure frequency remained the same as that before the surgery.	All patients decreased in the scores of Infrequency, Hypochondriasis, Psychasthenia and Schizophrenia in 1-year follow-up.
Rose, 1996 [25]	No comparative study	N=45	1 year	Minnesota Multiphasic Personality Inventory - adapted Neuroticism scale only was assessed.	SF=20, NSF=25	Changes in Neuroticism were not significant.

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Table 1 (continued)

First Author, year of publication, reference	Type of study	Sample	Period of follow-up	Evaluating of personality	Seizure outcome	Changes in personality after surgery
Wheelock, 1998 [31]	Comparative study, outcome of surgery (seizure free or not)	N=55, seizure-free N=24, not seizure free	2 months; 1 year	Minnesota Multiphasic Personality Inventory - only Depression and Psychasthenia scales were evaluated.	SF=55, NSF=24 reduction in seizures after surgery.	SF group showed improvements at both follow-ups;
Meier, 1965 [28]	Comparative study, surgery group vs non surgery group	N=38, temporal lobe epilepsy, of which: N=15 temporal lobectomy left; N=23 N=40, non-operated control group	1 year	Minnesota Multiphasic Personality Inventory; Two additional measures were included for analysis: the Caudality scale and an Index of Psychopathology.	N/A	Non-surgical group demonstrated no any changes in evaluated scales.

greater social desirability and self-control.

Another study [30] with follow-up periods of 1-month and 1-year reported a gradual decrease in scores for infrequency, hypochondriasis, psychasthenia, and schizophrenia at both evaluations, which only reached statistical significance at the one-year time point, and without changes between SF and NSF groups.

Another study [31] with a similar design, - two measures at 2 months and one year post-surgery - using only psychasthenia and depression scales, and found changes in both SF and NSF groups over time. The SF group showed reduced depression and psychasthenia throughout the entire follow-up, whereas the NSF group improved after 2 months but then returned to baseline after 1 year.

3.4. Neuroticism changes

Two of three evaluating neuroticism studies detected no changes in this personality dimension [25,23], but Witt et al. [27] found decreasing in a few subscales from the neuroticism global scale in SF group only.

4. Discussion

To our knowledge, this is the first systematic review investigating personality changes of PWE following ST. The discussion section is structured by the subsections reflecting personality changes in PWE following ST, according to postsurgical seizure outcome, localization of epileptogenic area to be resected, and duration of follow-up. Also, the neuroticism changes section is presented to focus on this important personality forming dimension which increased scores are linked with epilepsy according to the previous studies.

4.1. Localization of epileptogenic focus to be resected and personality changes

The localization of epileptogenic area influences the state of epilepsy, which might mean differences in neurophysiological outcome following ST. The insula is known to be involved in emotion formation and processing, and insula damage could lead to disruption in these functions. The insula resection group [26] had emotional disturbances postoperatively compared to the temporal cohort.

Three studies [23,8,27] detected no differences in personality features post-surgery when comparing a temporal group with an extra-temporal group. However, there were different personality changes in TLE patients with left compared to right lateralization [27,28]. Both groups demonstrated improvements in the same domains, but on different subscales. Despite the limitations and preoperative differences in neuropsychological features between groups [8], the common outcome seems robust and showed personality changes can depend on lateralization of epileptogenic area and only in the TLE.

4.2. Influence seizure freedom as a surgical outcome on changes in personality

Almost all studies found an association between seizure freedom and changes in the patients' personality. Seizures and interictal epileptic activity influenced epilepsy-specific personality domains such as organic psycho-syndrome and neuroticism [27], hypochondriasis [29], and psychasthenia [31]. Only one study [30] reported no changes between SF and NSF groups. However, despite the fact that the NSF group still had seizures, their seizure frequency was decreased by 75–90 % in 8 of 10 patients in this study. Thus, it could be inferred that reduction in seizure frequency, rather than complete seizure elimination, results in improved neuropsychological functioning in patients. Another study [31] found no difference in psychasthenia scores between SF and NSF groups in a short follow-up: both groups showed significant improvements on this scale meanings at the 1st postsurgical measure (2 months), but afterwards, only the NSF group declined to the baseline after 1 year. The difference between short and long-term data illustrates these personality features require more time to improve.

4.3. Longitudinal changes in studies with 2 time points

Whilst personality trait changes seem to be stable by one year post-surgery, the presence of further changes at two years shows that personality changes may be more gradual, and longer follow-ups may be required. Improvements are observed on both in clinical and truthfulness scales at both follow-up time points [32]. Gradual improvements on personality tests in 1-month and 1-year follow-ups was reported by another study [30]. Seizure freedom was associated with a stable improvement in psychasthenia at both follow-ups, whereas the NSF group improved after 2 months and then returned to the baseline after 1 year [31]. The authors explained these results in the NSF cohort as a consequence of positive expectations of ST and hope for improving seizure status later, despite continuing seizures in a short follow-up. Thus, we can conclude improvement in personality appears within a short follow-up period and the process continues within at least the first 2 years, and is mostly associated with seizure freedom.

4.4. Neuroticism changes

Two out of three measured neuroticism studies detected no changes in this dimension following surgery [25,23]. Witt et al. [27] found only a decrease in some subscales of this scale postoperatively in SF patients. The question of whether neuroticism is an epilepsy-driven feature remains open and needs clarifying by further research.

5. Limitations

The main limitation of the current systematic review is due to the different questionnaires that were applied for personality evaluation in

patients. Different approaches were used in the completion of these questionnaires: some studies used responses given by close relatives/friends while others used responses given by the patients themselves. Furthermore, different personality domains were evaluated. Also, both poorly adjusted personality traits and normal personality dimensions were evaluated. Different study designs were also applied: comparative studies, cohort studies, case-control studies. The studies varied widely in sample size and evaluated personality after different length follow-up periods. Finally, only articles written in English were reviewed.

6. Conclusions

Personality dimensions in PWE may change following ST. Personality traits became more adaptive due to decreased impulsivity, hypochondriasis, psychasthenia or increased control scales.

Three studies showed no changes in personality post-surgery, while one showed increased emotional lability, which was characterized as a negative development.

Studies comparing SF and NSF groups after surgery showed a decrease in poorly adjusted personality traits in SF patients, primarily organic psycho-syndrome and neuroticism, hypochondriasis, and psychasthenia.

Development of personality changes may be displayed within a short follow-up in both SF and NSF patients, but at further follow-up these improvements were only maintained in groups that were seizure-free.

What factors can lead to personality changes following ST of RE?

It follows from the definition, that personality is mediated by biological and environmental factors. There are many factors that may affect patients suffering from RE apart from the burden of the disease itself: side effects of medication, stigma, restrictions in social and professional activity, high-risk of complications in pregnancy and many more. Considerable decrease in seizure frequency in patients improves these factors, and decreases distress-level, which together lead to favorable changes in emotional and behavioral domains of personality.

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Declaration of Competing Interest

The authors report no declarations of interest.

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