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Self-injurious thoughts and behaviors in Russian patients with epilepsy: A prospective observational study

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ABSTRACT

Objective: A two-stage study aimed to estimate the prevalence of different types of self-injurious behaviors (suicidal ideation (SI), suicide attempts (SA), and nonsuicidal self-injury (NSSI)) in Russian patients with epilepsy (PWE), to identify factors associated with such behaviors, and to assess their impact on 3-year mortality.
Methods: We enrolled 459 consecutive adult PWE from two level 2 outpatient epilepsy centers in Moscow. The study consisted of two phases - first, we assessed all demographic and clinical characteristics and patients' history of SI, SA, and NSSI. In the second phase, three years after the initial screening, we analyzed patients' medical records to assess how self-injurious thoughts and behaviors were related to actual mortality.
Results: In our sample, the total lifetime and 12-month prevalence of SI was 20% and 5.7%, of SA was 8.3% and 0.7%, and of NSSI was 15.3% and 2.8%, respectively. We found no differences between deceased and alive PWE regarding lifetime and 12-month prevalence of SI, SA, and NSSI. Higher seizure frequency, lifetime NSSI and lifetime diagnosis of mental disorder were associated with SI, whereas traumatic brain injury (TBI), substance abuse, and NSSI were associated with SA in PWE.
Significance: Our study adds to the existing data on the prevalence of different types of suicidal behaviors in PWE and advances research on NSSI in this population. However, more research is needed on the long-term consequences of different types of self-injurious behaviors.

1. Introduction

Epilepsy is associated with many adverse social and clinical outcomes, including premature mortality [1]. The increased mortality is related not only to the cause of epilepsy (e.g., neoplasia, cerebrovascular disease), sudden unexpected death, status epilepticus, and accidents, but also to suicide [2,3]. For example, Nevalainen et al. found that suicide (RR 2.9, 95% CI 2.2–3.8) was the largest contributor to years of potential life lost (YPLL), accounting for 6.7% of excess YPLL due to epilepsy in the United States [4]. Suicidal ideation (SI) is associated not only with suicide-related mortality but also with all-cause mortality [5]. For example, in a primary care cohort of elderly patients, SI was associated with an increased risk of 5-year mortality even in those without depression [6]. A cohort study by Bergen et al. found that deaths from natural causes were 2 to 7.5 times more common in people presenting to emergency departments after self-poisoning or self-injury than in the general population [7]. In patients with chronic diseases, this can be explained by health-damaging behaviors, such as suboptimal medication adherence, which may be one of the possible underlying mechanisms for poorer prognosis [8]. In the most recent meta-analysis, the pooled prevalence of SI and suicide attempt (SA) in patients with epilepsy (PWE) was 23.2% and 7.4%, respectively [9]. In comparison, the cross-national study in 17 countries estimated the lifetime prevalence of SI at 9.2% and SA at 2.7% in the general population [10].

Several factors associated with suicidal behavior in PWE have been identified [3,7,8] including some epilepsy-specific characteristics (high seizure frequency [11], early onset of epilepsy [12], temporal lobe epilepsy [11], some antiseizure medications [13] and epilepsy surgery) [14,15]. In addition, variables such as perceived stigma [16], poor quality of life [17], mood [18] and anxiety disorders [19] significantly increase the risk of suicide.

Nevertheless, many proven predictors of suicidal behavior that have

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been identified in general population and specific clinical sample studies remain understudied in PWE. In contrast to general suicidology, well-known risk factors for suicidal behavior such as alternative gender identity [20], non-heterosexual orientation [21], bullying [22], and nonsuicidal self-injury (NSSI) [23] have received little attention in PWE studies [3]. This is surprising because NSSI behaviors, frequency of NSSI, and number of NSSI methods are the known predictors of SA [24]. Previous studies show that NSSI is common among individuals with chronic medical conditions and complaints [25,26]. In addition, the most common psychiatric comorbidity in both NSSI patients and PWE [27] is depression. A bidirectional relationship between depression and epilepsy has been proposed [17], but not all results from studies in this area support this hypothesis. For example, Cornaggia et al. did not find a significant association between epilepsy and severe depression [28].

The prevalence of suicidal behavior in PWE varies considerably from country to country. Cultural and economic circumstances and the characteristics of the health care systems in each country may explain this variability. For example, data on the prevalence of suicidal behavior in Russian PWE are scarce, but higher levels might be expected, as Russia has historically had higher suicide rates than most countries in the European region [29].

2. Aim

The primary objective of the study was to estimate the prevalence of SI, SA, and NSSI in Russian PWE. Secondary outcomes of the study were to identify variables associated with self-injurious thoughts and behaviors in PWE, and to examine whether PWE with these features are at higher risk of death in the 3-year period.

3. Patients and methods

The study design was approved by the Local Research Ethics Committee of the Moscow Research and Clinical Center for Neuropsychiatry, and all patients signed an informed consent form beforehand. The study consisted of two stages. The first phase of the study took place from September to December 2018. We enrolled 459 consecutive PWE aged 18 years and older from two level 2 outpatient epilepsy centers serving more than 4000 PWE in the South and Southwest districts of Moscow. All patients had at least two EEG scans and at least one MRI scan (or CT scan if MRI was not possible). Inclusion criteria were: (1) diagnosis of epilepsy according to the International League Against Epilepsy criteria, (2) age 18 years and older, (3) fluency in the Russian language, (4) residence in Moscow. Exclusion criteria were (1) cognitive impairment that prevented the patient from understanding the meaning of the questionnaires; (2) an epileptic seizure 48 h before completing the questionnaires. Patients with acute symptomatic seizures were not included in the study. elated to SI, SA, and NSSI. We took these questions from the Self-Injurious Thoughts and Behaviors Interview (SITBI) - the widely used tool for measuring the presence, frequency, and characteristics of suicidal and self-injurious thoughts and behaviors [30]. We used the first (basic) questions of the relevant parts of the tool: 1. Have you ever had thoughts of killing yourself? 2. Have you ever made an actual attempt to kill yourself in which you had at least some intent to die? 3. Have you ever purposely hurt yourself without wanting to die (for example, cutting or burning, but not taking into account cases when you had indirectly hurt yourself, for example, when you starved or got a tattoo/piercing)? In addition, patients reported when the thought or attempt last occurred. We extracted all epilepsy-related (e.g., age of onset, seizure type, antiseizure medication, etc.) and other medical (e.g., comorbidities) information from the «Unified Medical Information and Analytical System of Moscow» (EMIAS). This web-based information system contains information on all cases of health service utilization (medical check-ups, inpatient, outpatient, and medical emergency medical care) for all citizens of Moscow.

The second phase of the study took place from October 2021 to January 2022. We analyzed the patients' medical records for three years from the initial visit. We aimed to test the hypothesis that PWE involved in self-injurious thoughts and behaviors have a higher risk of death over a three-year period than non-involved PWE.

4. Statistical analysis

Descriptive analysis of demographic and clinical variables was performed. Continuous variables are presented as mean (standard deviation) and categorical variables as N (%), and the prevalence of SI, SA, and NSSI as% (95% CI).

Univariate associations of SI, SA, and NSSI with demographic and clinical variables were estimated using Fisher's exact test (for categorical variables) and Mann-Whitney U test (for continuous variables). The hypothesis of normality of the distribution of continuous variables (age, age at onset of epilepsy, and duration of epilepsy) was tested using the Kolmogorov-Smirnov test of normality. For all variables, the p-value was < 0.05, indicating an abnormal distribution. The Benjamini-Hochberg correction was used to correct for multiple comparisons of seizure type, ASM, aetiological, and comorbidity variables in this analysis [31, 32].

Variables with a p-value less than <0.05 were entered into general linear models to identify independent predictors of SI, SA, and NSSI. SI, SA and NSSI were entered as dependent variables in separate models, with categorical clinical and demographic variables as independent variables and continuous ones as covariates. Effect sizes for all independent variables and covariates were calculated using partial eta-squared (η2). Adjusted R-squared was calculated to assess the strength of association between the dependent variables and the predictor variables. All tests were two-tailed and statistical significance was set at $p < 0.05$. Models obtained from the inclusion of the adjusted variables are presented in Sup. 4.

Statistical processing was performed using Jamovi software v1.6.2. Calculations of descriptive statistics were performed in the Exploration module of Jamovi, 95% CI in the ESCI module, Mann-Whitney U test in the T-test module, Fisher's exact test in the Frequencies module, and the GAMLJ module was used for the general linear model.

5. Results

5.1. Sample characteristics

Of the 483 PWEs, 13 (2.7%) refused to participate in the study and 11 (2.3%) did not have the intellectual ability to read/understand the meaning of the questions asked. In the end, 459 consecutive PWEs 18 years and older were recruited into the study. The mean age of the patients was 45.2 (16.5) years; 258 (56.2%) were females assigned at birth. The mean age of epilepsy onset was 31.7 (19.6) years, and the mean duration of epilepsy was 13.4 (12.3) years. Most patients had focal-onset seizures, with 30.5% reporting more than 12 seizures per month and 39.9% seizure-free for 12 months or more. Almost two-thirds (64.1%) of patients received ASM monotherapy, 1.5% received no pharmacological treatment, and others were prescribed two or more ASMs. The most commonly used ASMs were carbamazepine (38.8%), levetiracetam (29%), and valproic acid (27.9%).

Demographic and clinical variables are presented in Table 1.

5.2. Prevalence of the self-injurious thoughts and behaviors

In the total sample, the overall lifetime prevalence rates for SI were 20% (95% CI 16.6–23.9%), for SA 8.3% (95% CI 6.1–11.2%), and for NSSI 15.3% (95% CI 12.3–18.8%).

In the past 12 months, 5.7% (95% CI 3.9–8.2%) of PWE had SI, 0.7% (95% CI 0.4–2.2%) had attempted suicide, and 2.8% (95% CI 1.6–4.8%) had NSSI.

Table 1
Socio-demographic and clinical variables of the sample.

	Mean (SD)/n (%)
Age (years)	45.2 (16.5)
Sex assigned at birth	
Male	201 (43.8%)
Female	258 (56.2%)
Education level	
Primary and secondary school education	80 (17.4%)
Vocational training	197 (42.9%)
Incomplete/complete higher education	182 (39.7%)
Employment	
EET*	167 (36.4%)
NEET**	292 (63.6%)
Marital status	
Single	168 (36.6%)
Registered marriage	198 (43.1%)
Divorced/Widowed	93 (20.3%)
Disability	
No	317 (69.1%)
Yes	142 (30.9%)
Age at onset of epilepsy (years)	31.7 (19.6)
Epilepsy duration (years)	13.4 (12.3)
Epilepsy type	
Focal	404 (88%)
Generalized	34 (7.4%)
Unspecified	21 (4.6%)
Seizure type	
Focal aware	145 (31.6%)
Focal impaired awareness	260 (56.6%)
Focal to bilateral tonic-clonic	284 (61.9%)
Generalized tonic-clonic	23 (5%)
Tonic-clonic with unknown onset	21 (4.6%)
Myoclonic	11 (2.4%)
Other	12 (2.6%)
Seizure frequency	
Seizure-free for 12 months and more	183 (39.9%)
1–11 per year	136 (29.6%)
2 and more per month	140 (30.5%)
Number of ASM	
0	7 (1.5%)
1	294 (64.1%)
2	126 (27.4%)
≥3	32 (7.0%)
ASM***	
Levetiracetam	133 (29.0%)
Carbamazepine	178 (38.8%)
Valproic acid	128 (27.9%)
Lamotrigine	79 (17.2%)
Topiramate	55 (12.0%)
Oxcarbazepine	31 (6.8%)
Eslicarbazepine	1 (0.2%)
Lacosamide	7 (1.5%)
Perampanel	4 (0.9%)
Gabapentine	3 (0.7%)
Pregabaline	2 (0.4%)
Phenobarbital/Benzobarbital	19 (4.1%)
Clonazepam	4 (0.9%)
Etiology of structural epilepsy	
Traumatic brain injury	74 (16.1%)
CVD (stroke and others)	61 (13.3%)
Brain tumors	45 (9.8%)
Neurodegenerative diseases	6 (1.3%)
Autoimmune diseases	8 (1.7%)
Neuroinfections	6 (1.3%)
Comorbidities	
Cerebral palsy	9 (2%)
HIV	7 (1.5%)
Heart diseases	71 (15.5%)
Joint diseases	4 (0.9%)
Allergies	7 (1.5%)
Arterial hypertension	162 (35.3%)
Diabetes mellitus	25 (5.4%)
Pulmonary diseases	28 (6.1%)
Cancer	38 (8.3%)
Gastrointestinal diseases	42 (9.1%)
Urinary system diseases	36 (7.8%)
Thyroid diseases	53 (11.5%)
Lifetime substance use disorder	32 (7%)
Lifetime mental disorder	150 (32.7%)

* In Education, Employment or Training;.
** Not in Education, Employment or Training;.
*** ASM – Antiseizure medication.

5.3. Suicidal ideation

In the univariate analysis, factors associated with SI were education level, age of epilepsy onset, seizure frequency, lifetime substance use disorder, mental disorder, and NSSI (Sup. 1).

In the multivariate analysis, factors that retained significance were seizure frequency (η2=0.022, $p = 0.014$), lifetime mental disorder (η2=0.028, $p < 0.001$), and lifetime NSSI (η2=0.056, $p < 0.001$). All factors included in the multivariate model accounted for 11.8% (R2=0.118) of the variance in predicting SI among PWE (Table 2).

The general linear model for SI with unadjusted variables (+ levetiracetam) is shown in Sup. 4. Pregabalin treatment was dropped from the model because of the low baseline rate.

5.4. Suicide attempts

In the univariate analysis, PWE with SA had a significantly lower level of education. Most of them had a disability group due to the epilepsy diagnosis. PWE with a history of TBI before epilepsy onset, lifetime substance use disorder, and NSSI were more likely to report SA (Sup. 2).

In multivariate analysis, history of TBI (η2=0.037, $p = 0.001$), lifetime substance use disorder (η2=0.028, $p < 0.001$), and NSSI (η2=0.078, $p < 0.001$) retained their significance. The overall model fit was adjusted R2=0.148, meaning that the factors in the model accounted for 14.2% of the variance of SA in PWE. (Table 2)

General linear model for SA with unadjusted variables (+ focal seizures, lifetime mental disorder) is represented in Sup. 4.

5.5. Nonsuicidal self-injurious behavior

Significant group differences were observed in the univariate analysis for SI and SA (Sup. 3).

After combining these factors in the general linear model, only SA

Table 2
General linear models for suicide ideation, suicide attempt and nonsuicidal self-injurious behavior.

Variable	Partial eta-squared	p-value	Adjusted R^2	p-value
Suicide ideation				
Education level	0.020	0.067	0.118	<0.001
Age at onset of epilepsy	0.009	0.84		
Seizure frequency	0.019	0.014		
Lifetime substance use disorder	0.018	0.051		
Lifetime diagnosis of mental disorder	0.027	<0.001		
Lifetime NSSI	0.056	<0.001		
Suicide attempt				
Education level	0.018	0.099	0.142	<0.001
Disability	0.010	0.155		
Traumatic brain injury	0.037	0.001		
Lifetime substance abuse	0.028	<0.001		
Lifetime NSSI	0.078	<0.001		
Nonsuicidal self-injurious behavior				
Lifetime suicide ideation	0.008	0.059	0.087	<0.001
Lifetime suicide attempt	0.035	<0.001		

(η2=0.035, $p < 0.001$) remained significantly associated with NSSI in PWE (Table 2). The overall model fit was adjusted R2=0.087.

5.6. Three-year mortality

Three years after the first evaluation, data from EMIAS were available for 444 patients. The main reason for missing data was a change of residence. Thirty-seven (8.3%: 95% CI 6.1–11.3%). PWE had died within three years. There were no deaths by suicide during the 3-year period. Twenty-six (5.9%: 95% CI 4.0–8.4%) died of natural causes, of which 7 (1.5%: 95% CI 0.7–3.2) were directly related to COVID-19. A further 11 PWE deaths were recorded as «undetermined manner of death», which is similar to the «open verdict» used in other countries.

We found no differences between the deceased and alive PWE regarding lifetime and 12-month prevalence of SI, SA and NSSI (Table 3).

6. Discussion

We revealed a higher prevalence of SI and SA in Russian PWE compared with data from general population studies [20]. Our results on lifetime prevalence of SI and SA are consistent with a recent meta-analysis, which showed a pooled prevalence of 23.2% (95% CI: 0.176–0.301) for SI and 7.4% (95% CI: 0.031–0.169) for SA [9]. The 12-month prevalence of SI in the study population was also high - 5.7% (95% CI 6.1–11.2%). Moreover, 0.7% (95% CI 0.4–2.2%) of patients in our sample met the DSM-5-TR duration criteria for current suicidal behavior disorder and were therefore at higher risk for recurrent SA.

NSSI is a significant public health concern in the Russian Federation, especially prevalent among youth and in certain clinical populations. In a study by Zinchuk et al., which either used SITBI, 60.1% of Russian patients with SI showed NSSI engagement [33]. Unfortunately, the data on NSSI in PWE are scarce, and we failed to find such data in Russian PWE. Although some types of self-harm behaviors have been studied previously in PWE with intellectual disabilities, the pathogenesis and functions of these behaviors differ significantly from the NSSI disorder as defined in the DSM-5-TR. One of the few studies addressing this issue revealed a higher prevalence of self-injurious behavior without suicidal intent (both cutting and overdose) in PWE (2.4%) compared with age- and sex-matched controls (1.5%) [34]. In our study, the prevalence of NSSI was higher (lifetime (15.3%: 95% CI 12.3–18.8%) and 12-month (2.8%: 95% CI 1.6–4.8%)) compared to those reported by Wirrell et al. [34].

Dispersion analysis revealed several factors associated with SI and SA. Lifetime NSSI was the most significant factor for both (η 2 = 0.056 for SI and η 2 = 0.078 for SA). Recent studies have shown that many characteristics such as negative affectivity [35], borderline personality traits [36], and dissatisfaction with parenting style [33] predict both NSSI and SI [37]. In terms of SA, NSSI behavior contributes to suicide capability by increasing habituation to pain and decreasing fearlessness about blood and injuring [38]. Another shared variable was lifetime substance abuse. Some studies on cohorts other than PWE have already shown an association between alcohol/substance abuse and both SI and SA [39,40].

Previous studies on suicidality have demonstrated the difference in the risk factors for SI and SA. In modern conceptions of suicide (e.g., the Three-Step Theory (3ST)), an «ideation-to-action» framework is implemented to find factors associated with the transition from SI to attempt [41]. Our data support this approach, revealing some variables that are exclusively related to ideation or attempts [42].

In PWE, lifetime mental disorders and epilepsy-related factors (seizure frequency) are associated with SI. Recent studies have shown that the prevalence of depression and anxiety [42] in Russian PWE is similar to or even higher than the results of meta-analyses [43]. For a long time, suicide was perceived as a consequence of mental disorders, but recent studies have shown that mental disorders can become an important cause of psychological distress and hopelessness, which contribute to the onset of SI, but are not directly related to SA [41]. Our data are consistent with these findings.

Higher seizure frequency was associated with SA in the study by Nilsson et al., while Friedman et al. did not find such an association, but revealed an association between poor seizure control and depressive symptoms [12,44]. Schabert et al. also found an association between poor seizure control and an increased risk of de novo mental disorders [45]. In our opinion, higher seizure frequency in PWE is associated with additional adverse factors besides depression, such as reduced ability to achieve professional and family goals, lower quality of life, and polypharmacy. This may facilitate the onset of SI.

While substance abuse has only borderline significance for SI, it is more strongly associated with SA. In the current literature, there is solid evidence of an association between alcohol consumption and an increased risk of epilepsy/unprovoked seizures [46] and depression [47]. Alcohol may be a cause of depression and additionally, it worsens the course of a mood disorder. Numerous studies have reported that substance abuse is strongly associated with many adverse outcomes, including suicide [48,49]. It has been calculated [50] that in Russia, a 1-liter increase in vodka sales would increase the suicide rate by 9.3% for men and 6% for women. Alcohol increases the propensity to act on SI through the disinhibition, impulsivity and impaired judgement [51] associated with both chronic and acute alcohol intoxication.

TBI has been another factor associated with SA. Recent meta-analyses [52] estimated a higher prevalence of suicidality in patients with TBI than in the general population. However, data on the relationship between suicidality and TBI in PWE are conflicting. While Robertson et al. [53] found no statistically significant association between suicidality and history of TBI, Boggs et al. [54] reported that both TBI (OR=23.53) and epilepsy (OR=3.17) were associated with significantly higher odds of suicide by firearm. Several possible explanations for the association between TBI and SA have been proposed, including abnormal structural connectivity [55] in brain regions critical for cognitive and emotional processing, and accumulation of

Table 3
Three-year mortality in PWE with and without self-injurious thoughts and behaviors (Fisher's exact test).

	All-cause mortality, N (%)			
	Total N-444	Dead N-37	Alive N-407	Dead/Alive, p-value
Lifetime SI*	86 (19.4%)	5 (13.5%)	81 (19.9%)	$p = 0.514$
12-month SI*	26 (5.9%)	2 (5.4%)	24 (5.9%)	$p = 1$
Lifetime SA**	34 (7.7%)	1 (2.7%)	33 (8.1%)	$p = 0.342$
12-month SA**	4 (0.9%)	0 (0%)	4 (1%)	$p = 1$
Lifetime NSSI***	64 (14.4%)	4 (10.8%)	60 (14.7%)	$p = 0.718$
12-month NSSI***	12 (2.7%)	2 (5.4%)	10 (2.5%)	$p = 0.264$

	Deaths with an unknown cause, N (%)			
	Total N-444	Unknown cause N-11	Alive + Natural causes death N-433	Dead/ Alive +Natural causes death, p-value
Lifetime SI*	86 (19.4%)	2 (18.2%)	84 (19.4%)	$p = 1$
12-month SI*	26 (5.9%)	1 (9.1%)	25 (5.8%)	$p = 0.489$
Lifetime SA**	34 (7.7%)	0 (0%)	34 (7.9%)	$p = 1$
12-month SA**	4 (0.9%)	0 (0%)	4 (0.9%)	$p = 1$
Lifetime NSSI***	64 (14.4%)	1 (9.1%)	63 (14.5%)	$p = 1$
12-month NSSI***	12 (2.7%)	0 (0%)	12 (2.8%)	$p = 1$

* SI – Suicide ideations.
** SA - Suicide attempts.
*** NSSI – Nonsuicidal self-injuries.

phosphorylated tau around blood vessels and at the depths of sulci in the prefrontal cortex, amygdala, and other brain regions that may be associated with depression and impulsivity [56]. It should be noted, that TBI and SA share similar risk factors. For example, impulsivity is associated with both TBI and SA [57,58], and it is possible that the TBI group has higher baseline impulsivity.

It is worth noting that, according to the results of a meta-analysis by Van Praag et al. [59], approximately 15% of TBI survivors develop post-traumatic stress disorder (PTSD), which in turn is a risk factor for the development of suicidality [60]. However, we did not find any mention of PTSD symptoms related to previous TBI in the EMIAS. This may be explained by the fact that TBI-associated PTSD may often go unrecognized in routine clinical practice in the general population [61].

Interestingly, the partial eta-squared of SA for NSSI was also high ($\eta 2 = 0.035$). Therefore, a bidirectional relationship between two variables is possible. Previously, the anti-suicide function ("responding to suicidal thoughts without actually attempting suicide") was described as one of the most common intrapersonal functions of NSSI [62].

In contrast to our expectations, SI, SA, and NSSI (both lifetime and current) failed to predict mortality in a three-year period since the first visit. This may be explained by the relatively high prevalence of structural epilepsy etiologies. Mortality is higher among those with such documented etiologies as cancer and cerebrovascular disease. We suggest that an additional study in patients with predominantly genetic or developmental etiology of seizures should be conducted to test whether suicidal thoughts and self-injurious behavior could predict mortality in PWE.

7. Limitations

First, the chosen method of screening for suicidal behavior can significantly affect the measured frequencies. We used the ultrashort screening method. Our strength was a self-report questionnaire: participants are more reluctant to report suicidal behavior to a medical worker sitting across. The greater sensitivity of self-reports for SI and suicidal behavior (minor type II error) has been found consistently in both adult and pediatric populations [63,64]. At the same time, paper forms are 2.7 times more likely to reveal NSSI behavior in PWE than electronic ones [65].

Secondly, the presence of mental disorders in PWE was established on the basis of medical records and not on the basis of structured clinical diagnostic interviews such as the MINI or SCID. The prevalence of mental disorders is highly dependent on how they are assessed. For example, according to a systematic review by Lu et al. (20–21), the prevalence of MDD was highest in the self-report questionnaire group (43.4%), followed by 21.8% in the clinical interview group and 13.0% in the medical database group [66]. Therefore, the use of databases may underestimate the true prevalence of mental disorders. We also did not report the psychiatric diagnoses themselves because a total of 13 nosographic forms were identified, making it difficult to assess their impact on the development of SI, SA and NSSI.

Because NSSI is common among people with mental disorders, particularly major depressive disorder, bipolar disorder, and borderline personality disorder, the power of this parameter might be reduced if the diagnoses themselves were included. However, according to a review by Hamza et al. , NSSI is an independent predictor of suicidal behavior [67].

Thirdly, neurologists referred patients with identified current SI to a psychiatrist, which could increase survival rates through the treatment of a comorbid mental disorder. At the same time, ignoring SI would be unethical because it would endanger the patient's life.

The fourth limitation of the study is the sample size. Perhaps some variables that showed marginal significance (e.g., substance use disorder for SI) would have been significant with more participants.

The fifth limitation is the high prevalence of structural epilepsy etiologies, which are associated with higher short-term mortality. Self-injurious thoughts and behaviors may be more predictive of a fatal outcome in PWE with a predominantly genetic or developmental etiology of seizures. In addition, several participants died from COVID-19. This may also influence the results, as a higher susceptibility to COVID-19 has been reported in people with mental and substance use disorders, which are also a significant risk factor for SI and attempt [68].

8. Conclusion

Suicidal and nonsuicidal self-injurious thoughts and behaviors are prevalent in Russian PWE. NSSI is tightly linked to SI and SA in PWE. Higher seizure frequency and lifetime mental disorder diagnosis are associated with SI. SA in PWE is associated with substance abuse and TBI. Further research into the pathogenesis of suicidality in patients with different forms of epilepsy may provide new data on mortality in this population and facilitate the development of appropriate prevention approaches.

Data availability statement

The data supporting the results of this study are available upon request from the corresponding author. The data are not publicly available due to privacy and ethical restrictions.

Declaration of Competing Interest

None of the authors have any conflicts of interest to disclose.

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Supplementary materials

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References

[1] Nevalainen O, Ansakorpi H, Simola M, Raitanen J, Isojärvi J, Artama M, et al. Epilepsy-related clinical characteristics and mortality: a systematic review and meta-analysis. Neurology 2014;83:1968–77. https://doi.org/10.1212/WNL.0000000000001005.

[2] Pompili M, Girardi P, Tatarelli R. Death from suicide versus mortality from epilepsy in the epilepsies: a meta-analysis. Epilepsy Behav 2006;9:641–8. https://doi.org/10.1016/j.yebeh.2006.06.019.

[3] Zinchuk MS, Avedisova AS, Pashnin EV, Voinova NI, Guekht AB. Suicidological research in epilepsy: problems of methodology. Zhurnal Nevrol i Psikhiatrii Im SS Korsakova 2019;119:23. https://doi.org/10.17116/jnevro201911911223.

[4] Nevalainen O, Simola M, Ansakorpi H, Raitanen J, Artama M, Isojärvi J, et al. Epilepsy, excess deaths and years of life lost from external causes. Eur J Epidemiol 2016;31:445–53. https://doi.org/10.1007/S10654-015-0095-5.

[5] Shiner B, Riblet N, Westgate CL, Young-Xu Y, Watts BV. Suicidal ideation is associated with all-cause mortality. Mil Med 2016;181:1040–5. https://doi.org/10.7205/MILMED-D-15-00496.

[6] Raue PJ, Morales KH, Post EP, Bogner HR, Ten Have T, Bruce ML. The wish to die and 5-year mortality in elderly primary care patients. Am J Geriatr Psychiatry 2010;18:341–50. https://doi.org/10.1097/JGP.0b013e3181c37cfe.

[7] Bergen H, Hawton K, Waters K, Ness J, Cooper J, Steeg S, et al. Premature death after self-harm: a multicentre cohort study. Lancet 2012;380:1568–74. https://doi.org/10.1016/S0140-6736(12)61141-6.

[8] Ammassari A, Antinori A, Aloisi MS, Trotta MP, Murri R, Bartoli L, et al. Depressive symptoms, neurocognitive impairment, and adherence to highly active antiretroviral therapy among HIV-infected persons. Psychosomatics 2004;45:394–402. https://doi.org/10.1176/appi.psy.45.5.394.

[9] Abraham N, Buvanaswari P, Rathakrishnan R, Tran BX, Thu GV, Nguyen LH, et al. A meta-analysis of the rates of suicide ideation, attempts and deaths in people with epilepsy. Int J Environ Res Public Health 2019;16. https://doi.org/10.3390/IJERPH16081451.

[10] Nock MK, Borges G, Bromet EJ, Alonso J, Angermeyer M, Beautrais A, et al. Cross-national prevalence and risk factors for suicidal ideation, plans and attempts. Br J Psychiatry 2008;192:98–105. https://doi.org/10.1192/BJP.BP.107.040113.

[11] Park S, Lee HB, Ahn MH, Park S, Choi EJ, Lee H, et al. Identifying clinical correlates for suicide among epilepsy patients in South Korea: a case–control study. Epilepsia 2015;56:1966–72. https://doi.org/10.1111/epi.13226.

[12] Nilsson L, Ahlbom A, Farahmand BY, Åsberg M, Tomson T. Risk factors for suicide in epilepsy: a case control study. Epilepsia 2002;43:644–51. https://doi.org/10.1046/J.1528-1157.2002.40001.X.

[13] Andersohn F, Schade R, Willich SN, Garbe E. Use of antiepileptic drugs in epilepsy and the risk of self-harm or suicidal behavior. Neurology 2010;75:335–40. https://doi.org/10.1212/WNL.0b013e3181ea157e.

[14] Pompili M, Girardi P, Tatarelli G, Angeletti G, Tatarelli R. Suicide after surgical treatment in patients with epilepsy: a meta-analytic investigation. Psychol Rep 2006;98:323–38. https://doi.org/10.2466/pr0.98.2.323-338.

[15] Zinchuk MS, Rider FK, Kustov GV, Pashnin EV, Akzigitov RG, Gudkova AA, et al. Suicidality in epilepsy: epidemiology and clinical risk factors. Zhurnal Nevrol i Psikhiatrii Im SS Korsakova 2018;118:45. https://doi.org/10.17116/jnevro201811810245.

[16] Lin M, Chen J, Li S, Qin Y, Wang X, Liu Y, et al. Risk factors for suicidal tendency in people with epilepsy in China: a case-control study. Sci Rep 2021;11. https://doi.org/10.1038/S41598-021-81870-9.

[17] AS Tedrus GM de, de Souza D de CM. I would be better off dead: investigating suicidal ideation in people with epilepsy. Arq Neuropsiquiatr 2022;80:718–24. https://doi.org/10.1055/s-0042-1755230.

[18] Rider FK, Danilenko OA, Grishkina MN, Kustov GV, Akzhigitov RG, Lebedeva AV, et al. Depression and epilepsy: comorbidities, pathogenesis, principles of therapy. Zhurnal Nevrol i Psikhiatrii Im SS Korsakova 2016;116:19. https://doi.org/10.17116/jnevro20161169219-24.

[19] Kanner AM, Saporta AS, Kim DH, Barry JJ, Altalib H, Omotola H, et al. Mood and anxiety disorders and suicidality in patients with newly diagnosed focal epilepsy: an analysis of a complex comorbidity. Neurology 2022. https://doi.org/10.1212/WNL.0000000000201671.

[20] Chew D, Tollit MA, Poulakis Z, Zwickl S, Cheung AS, Pang KC. Youths with a non-binary gender identity: a review of their sociodemographic and clinical profile. Lancet Child Adolesc Heal 2020;4:322–30. https://doi.org/10.1016/S2352-4642(19)30403-1.

[21] di Giacomo E, Colmegna F, Pescatore F, Aspesi F, Fotiadou M, Clerici M. The burden of personality disorders on the DSM 5 addiction to tobacco during pregnancy. Compr Psychiatry 2018;84:101–5. https://doi.org/10.1016/J.COMPPSYCH.2018.04.009.

[22] Holt MK, Vivolo-Kantor AM, Polanin JR, Holland KM, DeGue S, Matjasko JL, et al. Bullying and suicidal ideation and behaviors: a meta-analysis. Pediatrics 2015;135:e496. https://doi.org/10.1542/PEDS.2014-1864.

[23] Chesin MS, Galfavy H, Sonmez CC, Wong A, Oquendo MA, Mann JJ, et al. nonsuicidal self-injury is predictive of suicide attempts among individuals with mood disorders. Suicide Life-Threatening Behav 2017;47:567–79. https://doi.org/10.1111/sltb.12331.

[24] Victor SE, Klonsky ED. Correlates of suicide attempts among self-injurers: a meta-analysis. Clin Psychol Rev 2014;34:282–97. https://doi.org/10.1016/J.CPR.2014.03.005.

[25] Kim H, Ryu JM, Kim HW. Characteristics and trends of suicide attempt or non-suicidal self-injury in children and adolescents visiting emergency department. J Korean Med Sci 2020;35. https://doi.org/10.3346/JKMS.2020.35.E276.

[26] Eckert A, Domhardt M, Reinauer C, Berger G, Galler A, Böckmann A, et al. Non-suicidal self-injury in adolescents and young adults with type 1 diabetes: clinical characteristics from a German diabetes-patient registry (DPV). Psychiatry Res 2021;297. https://doi.org/10.1016/J.PSYCHRES.2021.113733.

[27] Mula M, Kanner AM, Jetté N, Sander JW. Psychiatric comorbidities in people with epilepsy. Neurol Clin Pract 2021;11:e112–20. https://doi.org/10.1212/CPJ.0000000000000874.

[28] Cornaggia CM, Beghi M, Beghi E. Psychiatric events in epilepsy. Seizure 2007;16:586–92. https://doi.org/10.1016/j.seizure.2007.04.006.

[29] World Health Organization. Suicide worldwide in 2019: global health estimates. World Heal Organ; 2021. Licence: CC BY-NC-SA 3.0 IGO.

[30] Nock MK, Holmberg EB, Photos VI, Michel BD. Self-injurious thoughts and behaviors interview: development, reliability, and validity in an adolescent sample. Psychol Assess 2007;19:309–17. https://doi.org/10.1037/1040-3590.19.3.309.

[31] Benjamini Y, Hochberg Y. Controlling the false discovery rate: a practical and powerful approach to multiple testing. J R Stat Soc Ser B 1995;57:289–300. https://doi.org/10.1111/J.2517-6161.1995.TB02031.X.

[32] Benjamini Y, Drai D, Elmer G, Kafkafi N, Golani I. Controlling the false discovery rate in behavior genetics research. Behav Brain Res 2001;125:279–84. https://doi.org/10.1016/S0166-4328(01)00297-2.

[33] Zinchuk M, Beghi M, Beghi E, Bianchi E, Avedisova A, Yakovlev A, et al. Non-suicidal self-injury in russian patients with suicidal ideation. Arch Suicide Res 2020:1–25. https://doi.org/10.1080/13811118.2020.1833801.

[34] Wirrell EC, Bieber ED, Vanderwiel A, Kreps S, Weaver AL. Self-injurious and suicidal behavior in young adults, teens, and children with epilepsy: a population-based study. Epilepsia 2020;61:1919–30. https://doi.org/10.1111/EPI.16618.

[35] Somma A, Fossati A, Ferrara M, Fantini F, Galosi S, Krueger RF, et al. DSM-5 personality domains as correlates of non-suicidal self-injury severity in an Italian sample of adolescent inpatients with self-destructive behaviour. Personal Ment Health 2019;13:205–14. https://doi.org/10.1002/pmh.1462.

[36] Peters EM, John A, Baetz M, Balbuena L. Examining the role of borderline personality traits in the relationship between major depression and nonsuicidal self-injury. Compr Psychiatry 2018;86:96–101. https://doi.org/10.1016/J.COMPPSYCH.2018.07.008.

[37] Flores-Kanter PE, García-Batista ZE, Moretti LS, Medrano LA. Towards an explanatory model of suicidal ideation: the effects of cognitive emotional regulation strategies, affectivity and hopelessness. Span J Psychol 2019;22. https://doi.org/10.1017/SJP.2019.45.

[38] May AM, Victor SE. From ideation to action: recent advances in understanding suicide capability. Curr Opin Psychol 2018;22:1–6. https://doi.org/10.1016/J.COPSYC.2017.07.007.

[39] Moradi Y, Dowran B, Sepandi M. The global prevalence of depression, suicide ideation, and attempts in the military forces: a systematic review and meta-analysis of cross sectional studies. BMC Psychiatry 2021;21. https://doi.org/10.1186/S12888-021-03526-2.

[40] Beghi M, Rosenbaum JF, Cerri C, Cornaggia CM. Risk factors for fatal and nonfatal repetition of suicide attempts: a literature review. Neuropsychiatr Dis Treat 2013;9:1725–36. https://doi.org/10.2147/NDT.S40213.

[41] Klonsky ED, Pachkowski MC, Shahnaz A, May AM. The three-step theory of suicide: description, evidence, and some useful points of clarification. Prev Med 2021;152. https://doi.org/10.1016/J.YPMED.2021.106549.

[42] Zinchuk M, Kustov G, Pashnin E, Gersamia A, Rider F, Yakovlev A, et al. Validation of the generalized anxiety disorder-7 (GAD-7) in Russian people with epilepsy. Epilepsy Behav 2021;123. https://doi.org/10.1016/J.YEBEH.2021.108269.

[43] Scott AJ, Sharpe L, Hunt C, Gandy M. Anxiety and depressive disorders in people with epilepsy: a meta-analysis. Epilepsia 2017;58:973–82. https://doi.org/10.1111/EPI.13769.

[44] Friedman D, Spruill TM, Liu H, Tatsuoka C, Stoll S, Jobst BC, et al. Depressive symptoms and suicidality among individuals with epilepsy enrolled in self-management studies: results from the US Centers for Disease Control and Prevention Managing Epilepsy Well (MEW) Network. Epilepsy Behav 2018;87:235–40. https://doi.org/10.1016/J.YEBEH.2018.06.024.

[45] Schabert VF, Stern S, Ferrari L, Wade CT, Willke RJ, Hauser WA. Incidence of mental health conditions by seizure control among adults with epilepsy in the United States. Epilepsy Behav 2022;134:108865. https://doi.org/10.1016/j.yebeh.2022.108865.

[46] Samokhvalov AV, Irving H, Mohapatra S, Rehm J. Alcohol consumption, unprovoked seizures, and epilepsy: a systematic review and meta-analysis. Epilepsia 2010;51:1177–84. https://doi.org/10.1111/J.1528-1167.2009.02426.X.

[47] Rehm J, Gmel GE, Gmel G, Hasan OSM, Imtiaz S, Popova S, et al. The relationship between different dimensions of alcohol use and the burden of disease-an update. Addiction 2017;112:968–1001. https://doi.org/10.1111/ADD.13757.

[48] Hawton K, Casañas I Comabella C, Haw C, Saunders K. Risk factors for suicide in individuals with depression: a systematic review. J Affect Disord 2013;147:17–28. https://doi.org/10.1016/J.JAD.2013.01.004.

[49] Amiri S, Behnezhad S. Alcohol use and risk of suicide: a systematic review and meta-analysis. J Addict Dis 2020;38:200–13. https://doi.org/10.1080/10550887.2020.1736757.

[50] Razvodovsky YE. Beverage-specific alcohol sale and suicide in Russia. Crisis 2009;30:186–91. https://doi.org/10.1027/0227-5910.30.4.186.

[51] Pompili M, Serafini G, Innamorati M, Dominici G, Ferracuti S, Kotzalidis GD, et al. Suicidal behavior and alcohol abuse. Int J Environ Res Public Health 2010;7:1392–431. https://doi.org/10.3390/IJERPH7041392.

[52] Chen F, Chi J, Niu F, Gao Q, Mei F, Zhao L, et al. Prevalence of suicidal ideation and suicide attempt among patients with traumatic brain injury: a meta-analysis. J Affect Disord 2022;300:349–57. https://doi.org/10.1016/J.JAD.2022.01.024.

[53] Roberson W, Rehman R, Bucurescu G. Antiepileptic drugs and suicidality in veterans with seizures. EC Neurol 2019;12:1–8.

[54] Boggs JM, Beck A, Hubley S, Peterson EL, Hu Y, Williams LK, et al. General medical, mental health, and demographic risk factors associated with suicide by firearm compared with other means. Psychiatr Serv 2018;69:677–84. https://doi.org/10.1176/APPI.PS.201700237.

[55] Aoki Y, Inokuchi R. A voxel-based meta-analysis of diffusion tensor imaging in mild traumatic brain injury. Neurosci Biobehav Rev 2016;66:119–26. https://doi.org/10.1016/J.NEUBIOREV.2016.04.021.

[56] Mez J, Daneshvar DH, Kiernan PT, Abdolmohammadi B, Alvarez VE, Huber BR, et al. Clinicopathological evaluation of chronic traumatic encephalopathy in players of american football. JAMA 2017;318:360–70. https://doi.org/10.1001/JAMA.2017.8334.

[57] Matei VP, Rosca AE, Pavel AN, Paun RM, Gmel G, Daeppen J-B, et al. Risk factors and consequences of traumatic brain injury in a Swiss male population cohort. BMJ Open 2022;12:e055986. https://doi.org/10.1136/bmjopen-2021-055986.

[58] Gvion Y, Apter A. Aggression, impulsivity, and suicide behavior: a review of the literature. Arch Suicide Res 2011;15:93–112. https://doi.org/10.1080/13811118.2011.565265.

[59] Van Praag DLG, Cnossen MC, Polinder S, Wilson L, Maas AIR. Post-traumatic stress disorder after civilian traumatic brain injury: a systematic review and meta-analysis of prevalence rates. J Neurotrauma 2019;36:3220–32. https://doi.org/10.1089/neu.2018.5759.

[60] Panagioti M, Gooding PA, Tarrier N. A meta-analysis of the association between posttraumatic stress disorder and suicidality: the role of comorbid depression. Compr Psychiatry 2012;53:915–30. https://doi.org/10.1016/j.comppsych.2012.02.009.
[61] Rosen V, Ayers G. An update on the complexity and importance of accurately diagnosing post-traumatic stress disorder and comorbid traumatic brain injury. Neurosci Insights 2020;15:263310552090789. https://doi.org/10.1177/2633105520907895.
[62] Klonsky ED, Glenn CR. Assessing the functions of non-suicidal self-injury: psychometric properties of the Inventory of Statements About Self-injury (ISAS). J Psychopathol Behav Assess 2009;31:215–9. https://doi.org/10.1007/S10862-008-9107-Z.
[63] Trivedi MH, Wisniewski SR, Morris DW, Fava M, Gollan JK, Warden D, et al. Concise Health Risk Tracking scale: a brief self-report and clinician rating of suicidal risk. J Clin Psychiatry 2011;72:757–64. https://doi.org/10.4088/JCP.11M06837.
[64] Vitiello B, Silva SG, Rohde P, Kratochvil CJ, Kennard BD, Reinecke MA, et al. Suicidal events in the treatment for adolescents with depression study (TADS). J Clin Psychiatry 2009;70:741–7. https://doi.org/10.4088/JCP.08M04607.
[65] Hesdorffer DC, French JA, Posner K, Diventura B, Pollard JR, Sperling MR, et al. Suicidal ideation and behavior screening in intractable focal epilepsy eligible for drug trials. Epilepsia 2013;54:879–87. https://doi.org/10.1111/EPI.12128.
[66] Gasparini S, Beghi E, Ferlazzo E, Beghi M, Belcastro V, Biermann KP, et al. Management of psychogenic non-epileptic seizures: a multidisciplinary approach. Eur J Neurol 2019;26:205–15. https://doi.org/10.1111/ENE.13818.
[67] Hamza CA, Stewart SL, Willoughby T. Examining the link between nonsuicidal self-injury and suicidal behavior: a review of the literature and an integrated model. Clin Psychol Rev 2012;32:482–95. https://doi.org/10.1016/j.cpr.2012.05.003.
[68] Taquet M, Luciano S, Geddes JR, Harrison PJ. Bidirectional associations between COVID-19 and psychiatric disorder: retrospective cohort studies of 62 354 COVID-19 cases in the USA. Lancet Psychiatry 2021;8:130–40. https://doi.org/10.1016/S2215-0366(20)30462-4.