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Clinical predictors of discordance between screening tests and psychiatric assessment for depressive and anxiety disorders among patients being evaluated for seizure disorders

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Abstract

Objective. To identify factors that predict discordance between screening instruments, the Neurological Disorders Depression Inventory for Epilepsy (NDDI-E) and Generalised Anxiety Disorder scale (GAD-7), and diagnoses made by qualified psychiatrists among patients with seizure disorders. Importantly, this is not a validation study, but rather investigates clinicodemographic predictors of discordance between screening tests and psychiatric assessment.

Methods. Adult patients admitted for inpatient video electroencephalogram monitoring (VEM) completed eight psychometric instruments, including NDDI-E and GAD-7, and psychiatric

assessment. Patients were grouped according to agreement between the screening instrument and psychiatrists' diagnoses. Screening was 'discordant' if the outcome differed from the psychiatrist's diagnosis, including both false positive and false negative results. Bayesian statistical analyses were used to identify factors associated with discordance.

Results. 411 patients met inclusion criteria; mean age was 39.6 years, and 55.5% (*n*=228) were female. Depression screening was discordant in 33% of cases (*n*=136/411), driven by false positives (*n*=76/136, 56%) rather than false negatives (*n*=60/136, 44%). Likewise, anxiety screening was discordant in one-third of cases (*n*=121/411, 29%) due to false positives (*n*=60/121, 50%) and false negatives (*n*=61/121, 50%). Seven clinical factors were predictive of discordant screening for both depression and anxiety: greater dissociative symptoms, greater patient-reported adverse events, subjective cognitive impairment, negative affect, detachment, disinhibition, and psychoticism. When the analyses were restricted to only patients with PNES or epilepsy, the rate of discordant depression screening was higher in the PNES group (*n* = 29, 47%) compared to the epilepsy group (*n* = 70, 30%, BF_{10} = f4.65).

Significance. Patients with seizure disorders who self-report a variety of psychiatric and other symptoms should be evaluated more thoroughly for depression and anxiety, regardless of screening test results, especially if they have PNES and not epilepsy. Clinical assessment by a qualified psychiatrist remains essential in diagnosing depressive and anxiety disorders among such patients.

Key words: Epilepsy; Seizures; Anticonvulsants; Nonepileptic seizures; Depression; Anxiety.

Introduction

People with epilepsy (PWE) and those with psychogenic non-epileptic seizures (pwPNES) have a high prevalence of depression and anxiety, and these contribute substantially to poor health-related quality of life, morbidity, and mortality.[1-4] A population-based case-control study revealed that comorbid psychiatric disease was the strongest risk factor for suicide in PWE, and a population-wide study reported that individuals with epilepsy and depression have 5 to 8 times the risk of suicide compared to non-depressed PWE.[3, 4] Similarly, a large cohort study found that 20% of deaths in pwPNES younger than 50 years were attributable to suicide and pwPNES younger than 30 years had an 8-fold increase in their standardised mortality rate.[5]

Given the significant deleterious impact of depression and anxiety on the wellbeing of PWE, prompt diagnosis of these comorbidities is crucial and may be facilitated through validated screening instruments.[6,7] Brief screening instruments, such as the Neurological Disorders Depression Inventory for Epilepsy (NDDI-E) and Generalised Anxiety Disorder Scale (GAD-7), have been validated for use in PWE and are widely used to screen for depression and anxiety.[8,9] The clinical factors that might lead to a discordant screening outcome, however, remain unclear.[10,11] For example, cognitive impairment is common in patients with seizure disorders, but it is not known whether cognitive impairment might lead people to misrepresent their true levels of psychopathology on a self-report measure.[12] The experience of adverse events, dissociative symptoms childhood trauma and psychoticism is common in pwPNES and may contribute to reporting of symptoms, but it is unknown if this affects screening instrument performance.[13-15]

We compared the outcomes of two screening instruments in patients being evaluated for seizure disorders, the NDDI-E and GAD-7, to the clinical diagnosis of a depressive or anxiety disorder made by a qualified psychiatrist in a cohort of patients admitted to video electroencephalogram monitoring (VEM) units for the evaluation of a suspected seizure disorder. We did not perform a validation study: instead, we investigated the clinical factors associated with discordant screening, with the latter including both false negative and false positive screening outcomes. We hypothesised that objective cognitive impairment would be associated with discordant screening outcomes, and that pwPNES would have higher rates of discordant screening due to greater symptom endorsement.[16]

Methods

Setting. Data were obtained from patients admitted to VEM units of the Comprehensive Epilepsy Programs at The Royal Melbourne Hospital and The Alfred Hospital, in Melbourne, Australia, between April 2018 and March 2020. The diagnostic procedures have previously been described.[17] Patients admitted for VEM undergo comprehensive epileptological and psychiatric assessments. Seizure- and medication-related clinical data were extracted from medical records.

Standard Protocol Approvals, Registrations, and Patient Consents. This study received approval from the Melbourne Health Human Research Ethics Committee and Alfred Health Ethics Committee (QA2012044 and 355/19, respectively).

Participants. Patients met inclusion criteria if they were aged 18 years or older, had been admitted to the VEM unit during the study period, and had complete data for the relevant variables. Patients not meeting all these criteria were excluded, as were those whose intellectual abilities precluded the completion of the required psychological instruments. Finally, patients with insufficient English to

complete the NDDI-E or GAD-7 were excluded as these instruments are not yet validated for use with an interpreter.

Diagnoses. Epilepsy was diagnosed in patients with two or more unprovoked seizures or a single seizure with an enduring seizure risk of >60%.[18] PNES diagnosis was determined by consensus opinion of epileptologists and psychiatrists at a multidisciplinary clinical meeting, following review of all available data.[19] Diagnosis required involuntary, sudden alterations in behaviour, sensation and/or motor activity linked to psychological or social distress, in the absence of electrographic ictal correlate. Comorbid epilepsy and PNES was diagnosed in some patients. Non-seizure diagnoses included migraine, vasovagal syncope, and cardiac events. Admissions were deemed non-diagnostic if inadequate data were collected to make either diagnosis (e.g. no events captured). All patients underwent clinical assessment by a qualified psychiatrist incorporating a thorough review of psychiatric symptoms, assessment of the developmental and psychosocial history, and collection of corroborative information from treating physicians and family members where appropriate. The final clinical diagnosis of a depressive or anxiety disorder was based on DSM-5 criteria for depression and anxiety, respectively.[20]

Psychometric instruments. Eight instruments are administered to all patients admitted to the VEM units as part of routine assessment and have been chosen for their reliability and ease of administration.

1. *NDDI-E.*[8] The NDDI-E was developed in 2006 as a screening instrument for major depression in epilepsy populations. It was initially validated for English-speaking populations in a cohort of 205 people recruited from five outpatient epilepsy clinics in the United States. It consists of six items: "everything is a struggle", "nothing I do is right", "feel guilty", "I'd be better off dead", "frustrated", and "difficulty finding pleasure". Symptoms that overlap with common side-effects of antiseizure medications were deliberately excluded to minimise the false positive rate in patients taking these medications. Patients select how often in the previous fortnight they were bothered by each symptom on a scale ranging from 1 (never) to 4 (always or often). For the primary analysis, a cut-off score of 15 was used to define positive cases. For secondary analyses (presented in supplementary materials), meta-analytic cut-off scores were used, where an NDDI-E score greater than 13 was considered 'positive' for depression.[21]

2. *GAD-7.*[22] The GAD-7 was developed in 2006 as a screening instrument for generalized anxiety disorder (GAD) and was validated in a cohort of 591patients recruited from 15 primary care clinics in the United States. It consists of seven items: "feeling nervous, anxious, or on edge", "not being able to stop or control worrying", "worrying too much about different things", "trouble relaxing", "being so restless that it is hard to sit still", "becoming easily annoyed or irritable", and

"feeling afraid as if something awful might happen". Patients select how often in the previous fortnight they were bothered by each symptom on a scale ranging from 0 (not at all) to 3 (nearly every day). A cut-off score of 10 was considered 'positive' for anxiety for the main analyses. Meta-analytic cut-off scores were used for the secondary analyses (presented in supplemental material), where a GAD-7 score greater than 8 was considered 'positive' for anxiety.[23]

3. *Neuropsychiatry Unit Cognitive Screening Tool (NUCOG)*.[24] The NUCOG is a validated, brief cognitive screening instrument developed by the Neuropsychiatry Unit of The Royal Melbourne Hospital, Australia. Scores range from 0-100, with lower scores indicating possible objective cognitive impairment.

4. *Quality of Life in Epilepsy Inventory (QOLIE-89).*[25] The QOLIE-89 is a validated, epilepsy-specific self-assessment tool evaluating quality of life, with higher scores indicating better subjective cognitive function.

5. *Liverpool Adverse Events Profile (LAEP)*.[26] The LAEP quantifies adverse events related to antiseizure medications. Using a scale from 1 to 4, where 4 denotes more frequent occurrence, patients score 19 different adverse events based on their experience over the preceding four weeks. A cumulative score of 45 or more is considered to represent a 'high toxicity' state.

6. *Wessex Dissociation Scale (WDS).*[27] The WDS quantifies how frequently a patient experiences dissociative symptoms. Developed in 2004, authors demonstrated adequate internal consistency and convergent validity with existing dissociation scales. The WDS comprises 40 items scored on a 6-point scale from "never" to "all the time". General dissociation as well as trauma-associated dissociation symptoms are assessed. Higher scores are suggestive of a dissociative disorder.

7. *Childhood Trauma Questionnaire (CTQ)*.[28] The CTQ is a validated 28-item instrument rating the severity of five sub-categories of trauma: emotional abuse, emotional neglect, physical abuse, physical neglect, and sexual abuse. Patients are asked to consider their experiences only prior to the age of 17 and assign each item a score from 1 (not at all traumatic) to 7 (extremely traumatic). Total sub-category scores correlate with trauma severity from 'none' to 'severe'.

8. *Personality Inventory for DSM-5 (PID-5)*.[29] The PID-5 is a 220-item patient-reported instrument created to assess personality traits. Each item is ranked on a 4-point scale from 0 (very false) to 3 (very true). A total of 25 traits facets are assessed (e.g. grandiosity, impulsivity). Results produce indices of five broad trait domains: negative affect, detachment, antagonism, disinhibition, and psychoticism.

Seizure frequency scale. An average seizure frequency over the 12 months prior to VEM admission was calculated. PWE were given a score on a 13-point scale used in previous studies where 0 describes patients who are seizure-free without antiseizure medications and 12 denotes a patient in status epilepticus.[30] This scale was adapted to describe event frequency in order to quantify disease severity among pwPNES.

Data Availability. Anonymised data, and the standardised proforma used to extract information on patient demographics and clinical characteristics, will be shared by request from any qualified investigator.

Statistical analyses

All statistical analyses were performed using the R (R Core Team, 2019) and JASP (JASP team, 2020) software packages. Bayesian contingency table analyses were used to test the null hypothesis of independence between two categorical variables.[31] Effect sizes, in the form of log odds ratios, were reported for 2x2 table along with 95% credible intervals (CIs). Bayesian independent samples t-test were used to compare the means of continuous variables between two groups.[32] Standardised effects sizes, in the form of Cohen's d, were computed and reported as the median of the posterior probability distribution along with 95% highest posterior density intervals (HPDI).[33] All independent samples t-tests were repeated using a Bayesian implementation of the Mann-Whitney test to ensure robustness to distributional assumptions.[34] Missing data were dealt with via pair-wise deletion. Hypothesis testing was performed by computation of the Bayes factor for the alternative hypothesis (BF_{10}), which represents the ratio of evidence for the alternative hypothesis over the null hypothesis. We considered $BF_{10} > 3.2$ as an approximate lower bound of evidence for the alternative hypothesis.[35] Conversely, $BF_{10} < 1/3.2$ was taken as a convenient boundary for evidence supporting the null hypothesis.[35] BF_{10} values between approximately 1/3.2 and 3.2 were considered insensitive to either hypothesis given the evidence. Follow-up logistic regression analyses were performed to investigate the specific NDDI-E and GAD-7 items that contributed to discordant screening results for depression and anxiety. The screening outcome (discordant versus concordant) was entered as the dependent variable, while the individual questionnaire items were added as the independent variables.

Results

Sample characteristics

Of the 521 patients who attempted psychometric instruments during the study period, 42 were excluded due to inadequate proficiency in English. A further six were excluded due to being aged less than 18 years old, and 62 were excluded because they had not completed the NDDI-E or GAD-7

(Figure 1). The final sample comprised 411 patients *(Table 1)*. The most common VEM diagnosis was epilepsy (*n*=234/411, 57%), followed by PNES (*n*=62/411, 15%), other non-epileptic events (*n*=30/411, 7%), and concomitant PNES and epilepsy (*n*=25/411, 6%). A diagnosis could not be reached in 60 cases (*n*=60/411, 15%).

Of the total cohort, approximately one-third of patients were diagnosed with a depressive disorder following psychiatric evaluation (*n*=133/411, 32%). A similar proportion received a diagnosis of an anxiety disorder (*n*=126/411, 31%), with some patients receiving both diagnoses (*n*=59/411, 14%). Bayesian contingency table analyses demonstrated that the proportion of depression diagnoses (BF_{10} = 0.02) did not vary across VEM diagnostic groups, while the analysis for anxiety was insensitive (BF_{10} = 1.62).

Screening concordance

The screening outcome for depression was concordant in the majority of cases (*n*=275/411, 67%). Of the cases that screened discordantly for depression (*n*=136, 33%), the majority were false positives (n=76/136, 56%) rather than false negatives (n=60/136, 44%) *(Figure 1)*. Similarly, the screening outcome for anxiety was concordant in the majority of cases (*n*=290/411, 71%). The discordant cases were equally likely to be false positives (n=60/121, 50%) and false negatives (n=61/121 50%) *(Figure 1)*. A comparable pattern was observed when using the meta-analytic cut-off scores (*Table S1*, *Figure S1*).

Factors associated with screening errors

As shown in *Table 2*, neither VEM diagnosis nor sex was associated with discordant screening for depression or anxiety. When the analyses were restricted to only patients with PNES or epilepsy, the rate of discordant depression screening was higher in the PNES group (*n* = 29, 47%) compared to the epilepsy group (*n* = 70, 30%, BF_{10} = 4.65). It was unclear on the evidence, however, whether this was driven by false negative or false positive screening outcomes.

The variables associated with screening concordance for depression are shown in *Table 3*. Discordant screening was associated with greater endorsement of dissociative symptoms, childhood trauma, greater patient-reported adverse events, negative affect, detachment, disinhibition, and psychoticism. Patients who screened discordantly for depression also reported poorer subjective cognition. Age at admission, disease duration, seizure frequency, number of prescribed antiseizure medications, objective cognitive function, and levels of antagonism were not associated with screening concordance.

As shown in *Table 4*, a similar pattern was observed when just considering the depression false negative screening outcomes. False negative screening tests were associated with higher levels of dissociation, childhood trauma, negative affect, detachment, disinhibition, and psychoticism. Patients with true negative screening tests reported better subjective cognition, but there was no evidence for a commensurate relationship with objective cognition. As shown in *Table 5*, no factors were predictive of false positive depression screening tests.

The variables associated with discordant anxiety screening are shown in *Table 3*. Discordant screening was associated with higher dissociation, greater patient-reported adverse events, poorer subjective cognition, negative affect, detachment, disinhibition, and psychoticism. As for depression, objective cognition was not a factor. False negative anxiety screening tests were associated with a younger age at admission, greater dissociative symptoms, childhood trauma, negative affect and psychoticism (*Table 4*). As for depression, no factors were associated with false positive anxiety screening tests (*Table 5)*.

All analyses were repeated using the meta-analytical cut scores. These findings were generally comparable and are included in the supplementary materials (*Table S2-S4*).

Follow-up analyses revealed that item 5 of the NDDI-E ('Frustrated') was particularly associated with discordant depression screening outcomes (*Table S5*). For every 1-point increase in this item, the odds of a discordant screening result increased by 1.58 (95%CI = 1.12, 2.23). For anxiety, item 5 of the GAD-7 ('Being so restless that it is hard to sit still') was particularly associated with discordant anxiety screening outcomes. For every 1-point increase in this item, the odds of a discordant anxiety screening result increased by 1.58 (95%CI = 1.16, 2.15).

Discussion

The results of this study demonstrate that screening instruments for anxiety and depression among patients being evaluated for seizure disorders can be unreliable, particularly in certain patient subgroups. Discordant screening results for both disorders were seen among patients with greater dissociative symptoms, higher patient-reported adverse events, poorer subjective cognition, negative affect, detachment, disinhibition, and psychoticism. False negative screening tests may incorrectly reassure clinicians that patients do not have a depressive or anxiety disorder, when in fact they do have a psychiatric illness associated with significant morbidity and mortality. To minimise 'missed diagnoses' due to false negative screening tests, clinicians should be sceptical of 'normal' anxiety and depression screening results among patients with higher levels of dissociation, a history of childhood trauma, negative affect, or psychoticism. Certain additional factors are predictive of false negative

depression screening (poorer subjective cognition, detachment, and disinhibition) while younger age is associated with false negative screening for anxiety. Importantly, many of these factors are common in pwPNES, which may account for the higher rates of discordant depression screening among this group. Although screening instruments for depressive and anxiety disorders are convenient and easy to administer without specialised training, clinicians should be aware of their limitations among certain patient populations.

Patients reporting poorer cognition were more likely to have discordant screening results for anxiety and depression. Conversely, objective cognition was not predictive of diagnostic concordance. In other words, screening outcomes were more likely to be discordant among patients who complained of cognitive impairment, but who did not necessarily have impaired cognitive function on testing. Impaired cognitive insight is thought to suggest a more pervasive lack of insight into one's mental processes, which includes mood and anxiety symptoms, with previous research showing subjective cognitive complaints to be strongly associated with anxiety and depression in PWE.[36]

Higher rates of patient-reported adverse events were predictive of discordant screening results for both depressive and anxiety disorders. It is unclear whether this was driven by false negative or false positive results. On the one hand, a higher adverse event reporting rate may represent somatisation of an underlying depressive or anxiety disorder. Somatisation and other atypical manifestations of anxiety and depression are poorly captured by standard screening instruments. Conversely, patients who report more adverse events may have a general tendency for over-endorsement, resulting in false positive screening outcomes.

Three psychometric variables were predictive of discordant screening for both depression and anxiety: dissociation, detachment, and psychoticism. Dissociation, defined as a failure to integrate experiences, is known to alter the phenomenology of many psychiatric disorders.[37] The fragmentary nature of dissociation may confound attempts at diagnosis based on 'typical' features of depressive and anxiety disorders included on screening tests.[38] Previous studies have identified that depressed patients with dissociation symptoms have distinct clinical features, such as more psychosocial-related symptoms (e.g., fear of abandonment, unstable relationships).[39,40] In light of these differences, some have suggested that 'dissociative depression' be a distinct diagnostic subtype.[41] Our results support this suggestion: the NDDI-E poorly captured the atypical depressive symptoms experienced by those with dissociation symptoms. Detachment is a maladaptive personality construct characterised by withdrawal and intimacy avoidance. These general personality traits are not necessarily indicative of clinical depression or anxiety but are reflected by items on the NDDI-E (e.g. difficulty finding pleasure) and GAD-7 (e.g. feeling afraid as if something awful might happen) thus reducing these items' validity at detecting underlying psychiatric illness. Psychoticism is a personality trait

associated with unusual beliefs and experiences, and perceptual dysregulation.[29] Such patients' eccentricity may lead to their failure to identify with depression or anxiety symptoms included in screening tests.

Patients with a history of childhood trauma, and negative affect were more likely to screen falsely negative for both depression and anxiety. Such patients may develop coping mechanisms to manage the pervasive emotional distress associated with the abnormal personality construct of affective negativity, or trauma. When successful deployed, these coping mechanisms may attenuate the symptoms of depression and anxiety such that they no longer cause the functional impairment required for a diagnosis. However, maladaptive emotional suppression may result in a failure to endorse depressive and anxiety symptoms on screening tests, despite their underlying presence. Childhood trauma disrupts development across psychological, physiological, and social domains with far-reaching impacts on mood, self-regulation, and behaviour.[42,43] Diagnosis of the complex psychiatric impact of childhood trauma relies on expert, individualised assessment; clinicians should be mindful that this trauma may impact the reliability of screening instruments.

Higher rates of disinhibition were seen among patients with negative screening results who were ultimately diagnosed with depression. Disinhibition describes a tendency towards impulsivity and a disregard for social norms. Consequently, disinhibited patients may be less likely to endorse the NDDI-E item 'nothing I do is right' due to individually determined norms that differ from social conventions of 'right' and 'wrong'.

Younger patients were more likely to have false negative anxiety screening outcomes. This may reflect a reluctance to endorse anxiety symptoms due to perceived social stigma. In an anonymous survey of 386 American college students, one-third thought it would be 'embarrassing' to seek mental health treatment; one-third also believed that their peers would 'treat them differently'.[44]

Limitations

Our patient cohort was recruited from patients admitted to VEM units, which may limit generalisability to other settings. PWE requiring VEM admissions generally have more severe disease, so may not be representative of all PWE. However, this increased disease complexity means that patients within our cohort have a broader range of cognitive function, type and number of antiseizure medications, and epilepsy aetiology. In clinical practice, patients being investigated for seizure disorders are often screened for depressive and anxiety disorders upon admission to a VEM unit, before a diagnosis of PNES or epilepsy, for example, is made. For those patients in whom epilepsy is not ultimately diagnosed, their NDDI-E result – being an instrument only validated among PWE – is of limited validity. Nevertheless, we feel that our approach reflects real-world practice and

allows VEM unit clinicians to identify patients who are 'at risk' of discordant depressive or anxiety disorder screening based on clinicodemographic factors, regardless of their ultimate seizure disorder diagnosis. Further, as recommended in the NDDI-E development paper, all patients underwent AE screening with the Liverpool AEP to provide complementary data for NDDI-E interpretation. While in our study VEM diagnosis had no bearing on the rate of diagnostic discordance overall, when considering just the epilepsy and PNES groups (i.e., excluding non-diagnostic admissions and non-seizure diagnoses), the latter had a higher rate of discordant depression diagnoses. Further research is warranted in this area, particularly as depression is a driving force for a higher mortality rate among pwPNES.[3-5] When the NDDI-E was developed and validated, subjects had to have a 4th grade reading level to minimize errors in the interpretation of the six items [8] While IQ testing was not one of the eight psychometric instruments administered to all patients, we did exclude any patients with a known intellectual disability or reading impairment. The formal psychiatric evaluation covered all major (axis 1) disorders. While dissociative disorders were investigated in all patients, we could not systematically incorporate this information into our statistical analyses; it is possible that PWE scored the loss of awareness in a focal seizure as a dissociative episode**.**

Conclusion

This study reveals that commonly used screening instruments for anxiety and depression in patients with seizure disorders have a high rate of discordance with gold-standard psychiatric evaluation among certain patient populations. The clinical utility of these screening instruments may be reduced in those with greater dissociative symptoms, higher patient-reported adverse events, poorer subjective cognition, negative affect, detachment, disinhibition, and psychoticism. Certain additional factors are predictive of false negative depression screening (poorer subjective cognition, detachment, and disinhibition) while younger age is associated with false negative screening for anxiety. Neurologists need to bear in mind that screening instruments may miss depressive and anxiety disorder diagnoses in these patient subsets; it may be prudent to proceed directly to formal psychiatric evaluation if these clinicodemographic factors are identified. Similarly, the higher rates of discordant depression screening among pwPNES compared to PWE highlights the need for formal psychiatric evaluation in this patient subset, regardless of screening test results. Future research directions may include examining other screening instruments that more accurately capture anxiety and depression in these patient subsets.

Key point box:

- Depression and anxiety are highly prevalent among those with seizure disorders and are associated with increased morbidity and mortality

- Screening can identify those with anxiety and depression, but results can be discordant with psychiatric assessment in certain subgroups
- Predictors of discordant screening included dissociative symptoms, poor subjective cognition, detachment, disinhibition, and psychoticism
- These patients should be thoroughly evaluated for depression and anxiety, especially if they have PNES and not epilepsy

Disclosure of conflicts of interest

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We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines

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Table 1. Sample characteristics – *Mean* (*SD*)

Outcome	VEM diagnosis					Total (n = 411)
	Epilepsy (n = 234)	PNES (n = 62)	PNES + Epilepsy (n = 25)	Other non-epileptic events (n = 30)	Non-diagnostic (n = 60)	
Clinicodemographic						
Female – *n* (%)	125 (53%)	41 (66%)	13 (52%)	19 (63%)	30 (50%)	228 (55%)
Age at admission – years	39.29 (15.48)	36.98 (14.51)	39.38 (12.74)	40.80 (18.35)	42.73 (16.39)	39.57 (15.56)
Disease duration – years	15.18 (12.74)	7.18 (10.65)	20.80 (17.47)	7.73 (9.40)	7.33 (10.06)	12.63 (12.88)
Seizure frequency	6.67 (1.93)	6.61 (2.28)	6.28 (2.30)	5.63 (2.27)	5.88 (2.08)	6.45 (2.08)
Number of antiseizure medications prescribed on admission	2.29 (1.14)	0.69 (0.97)	2.48 (1.16)	0.43 (0.57)	0.55 (0.83)	1.67 (1.33)
Psychiatric						
Depressive disorder – *n* (%)	73 (31%)	24 (39%)	15 (60%)	5 (17%)	21 (35%)	133 (32%)
Anxiety disorder – *n* (%)	60 (26%)	29 (47%)	11 (44%)	8 (27%)	18 (30%)	126 (31%)
Psychometric						
Depression	13.24 (4.72)	15.85 (4.56)	13.04 (3.47)	13.27 (4.53)	12.98 (4.48)	13.59 (4.66)
Anxiety	7.15 (5.74)	10.77 (6.22)	8.28 (5.68)	7.77 (6.37)	6.67 (5.44)	7.74 (5.94)
Dissociation	79.40 (30.47)	37.24 (48.00)	83.68 (44.00)	75.18 (41.00)	79.57 (32.39)	82.62 (32.10)
Childhood trauma	35.70 (13.75)	48.40 (21.39)	41.18 (14.21)	32.85 (8.99)	37.34 (16.58)	38.25 (16.30)
LAEP (antiseizure	41.93	49.45	44.09	45.21	43.72	43.74

medication adverse events)	(12.12)	(9.76)	(10.26)	(11.55)	(11.32)	(11.77)
Subjective cognition	80.01 (21.89)	71.00 (21.25)	76.74 (25.75)	75.86 (20.89)	83.41 (23.77)	78.67 (22.44)
Objective cognition	84.71 (11.94)	88.95 (8.02)	87.75 (8.23)	87.79 (9.01)	87.76 (8.07)	86.15 (10.67)
Negative affect	1.07 (0.63)	1.30 (0.82)	1.27 (0.64)	1.01 (0.72)	0.91 (0.57)	1.09 (0.67)
Detachment	0.85 (0.59)	0.96 (0.61)	0.93 (0.53)	0.64 (0.55)	0.80 (0.66)	0.85 (0.60)
Antagonism	0.51 (0.42)	0.38 (0.40)	0.59 (0.54)	0.38 (0.33)	0.39 (0.36)	0.47 (0.41)
Disinhibition	0.78 (0.53)	0.95 (0.52)	0.87 (0.41)	0.69 (0.50)	0.82 (0.52)	0.82 (0.52)
Psychoticism	0.62 (0.52)	0.88 (0.59)	0.86 (0.53)	0.58 (0.52)	0.55 (0.49)	0.66 (0.54)

PNES = psychogenic non-epileptic seizures.

Table 2. Screening discordance by VEM diagnosis, and sex

	VEM diagnosis						*Sex*		
Variable	*Epilepsy*	*PNES*	*PNES + Epilepsy*	*Other non-epileptic events*	*Non-diagnostic*	BF_{10}	*Female*	*Male*	BF_{10}	*log(OR) [95% Cis]*
Depression										
Discordant	70 (30%)	29 (47%)	12 (48%)	7 (23%)	18 (30%)	0.21#	83 (36%)	53 (29%)	0.41	-0.33 [-0.75, -0.08]
False negative	29 (41%)	10 (34%)	8 (67%)	2 (29%)	11 (61%)	0.03#	33 (40%)	27 (51%)	0.09#	0.01 [-0.54, 0.55]
False positive	41 (59%)	19 (66%	4 (33%)	5 (71%)	7 (39%)	0.03#	50 (60%)	26 (49%	0.55	-0.48 [-1.01, -

		)						)		0.04]
Anxiety										
Discordant	58 (25%)	23 (37%)	9 (36%)	12 (40%)	19 (32%)	0.04#	71 (31%)	50 (27%)	0.16#	-0.18 [-0.60, 0.25]
False negative	29 (50%)	9 (39%)	6 (67%)	5 (42%)	12 (63%)	0.01#	41 (58%)	20 (40%)	0.68	-0.58 [-1.15, 0.01]
False positive	29 (50%)	14 (61%)	3 (33%)	7 (58%)	7 (37%)	0.10#	30 (42%)	30 (60%)	0.14#	0.28 [-0.25, 0.82]

Note: BF_{10} = The Bayes factor for the alternative hypothesis. # indicates $BF_{10} < 1/3$, which provides support for the null hypothesis. *%* = percentage within category, e.g., % discordant for depression in epilepsy is derived from the sum of concordant and discordant. % of false negative is derived using the number discordant as the denominator.

Table 3. Concordant vs discordant screening outcomes for depression and anxiety.

	Mean (SD)			
Variable	*Concordant*	*Discordant*	*BF_{10}*	*d [95% HPDIs]*
Depression				
Clinicodemographic				
Age at admission	40.21 (15.78)	38.27 (15.07)	0.22#	-0.12 [-0.32, 0.08]
Disease duration	12.34 (12.73)	13.21 (13.20)	0.14#	0.07 [-0.14, 0.23]
Seizure frequency	6.49 (2.02)	6.36 (2.20)	0.14#	-0.06 [-0.26, 0.14]
ASMs	1.64 (1.31)	1.74 (1.38)	0.15#	0.07 [-0.13, 0.27]
Psychometric				
Dissociation	76.44 (29.56)	95.74 (33.43)	>100*	0.61 [0.39, 0.83]
Childhood trauma	36.02 (14.79)	41.79 (17.35)	19.63*	0.36 [0.14, 0.59]
AEs	41.80 (12.08)	47.84 (9.95)	>100*	0.51 [0.29, 0.73]
Subjective cognition	81.78 (21.90)	71.93 (22.19)	>100*	-0.43 [-0.65, -0.22]
Objective cognition	86.78 (9.51)	84.86 (12.64)	0.45	-0.17 [-0.38, 0.04]

Negative affect	0.99 (0.66)	1.31 (0.64)	>100*	0.47 [0.25, 0.70]
Detachment	0.79 (0.60)	0.99 (0.59)	9.00*	0.33 [0.11, 0.56]
Antagonism	0.45 (0.40)	0.51 (0.44)	0.24#	0.13 [-0.10, 0.35]
Disinhibition	0.75 (0.51)	0.96 (0.49)	59.40*	0.40 [0.18, 0.63]
Psychoticism	0.57 (0.51)	0.87 (0.55)	>100*	0.57 [0.34, 0.80]
Anxiety				
Clinicodemographic				
Age at admission	40.43 (16.17)	37.50 (13.84)	0.52	-0.18 [-0.39, 0.03]
Disease duration	12.51 (12.41)	12.91 (14.01)	0.12#	0.03 [-0.18, 0.24]
Seizure frequency	6.48 (2.06)	6.37 (2.14)	0.13#	-0.05 [-0.23, 0.16]
ASMs	1.74 (1.36)	1.51 (1.26)	0.40	-0.17 [-0.38, 0.04]
Psychometric				
Dissociation	78.44 (30.28)	92.85 (34.22)	>100*	0.44 [0.22, 0.67]
Childhood trauma	36.78 (15.68)	40.53 (16.10)	0.96	0.23 [-0.01, 0.46]
AEs	42.30 (11.97)	47.20 (10.53)	90.56*	0.41 [0.19, 0.63]
Subjective cognition	81.09 (21.41)	72.68 (23.86)	28.65*	-0.37 [-0.59, -0.15]
Objective cognition	86.24 (10.91)	85.93 (10.09)	0.13#	-0.03 [-0.24, 0.19]
Negative affect	1.03 (0.68)	1.25 (0.63)	5.75*	0.32 [0.09, 0.55]
Detachment	0.79 (0.57)	1.00 (0.66)	9.06*	0.34 [0.11, 0.57]
Antagonism	0.46 (0.41)	0.48 (0.42)	0.14#	0.05 [-0.18, 0.28]
Disinhibition	0.77 (0.51)	0.77 (0.51)	5.58*	0.32 [0.09, 0.55]
Psychoticism	0.59 (0.52)	0.84 (0.55)	>100*	0.44 [0.21, 0.68]

Note: BF_{10} = The Bayes factor for the alternative hypothesis. * indicates $BF_{10} > 3$, which provides support for the alternative hypothesis. # indicates $BF_{10} < 1/3$, which provides support for the null hypothesis. *D* = Cohen's d. *HPDI* = highest posterior density intervals. ASM = antiseizure medication. AEs = patient-reported adverse events.

Table 4. Depression and anxiety true negatives vs false negatives.

	Mean (SD)			
Variable	*True negative*	*False negative*	*BF_{10}*	*d [95% HPDIs]*
Depression				
Clinicodemographic				

Age at admission	39.83 (15.99)	39.75 (16.47)	0.16#	0.00 [-0.27, 0.28]
Disease duration	11.91 (12.85)	13.47 (14.86)	0.21#	-0.11 [-0.39, 0.17]
Seizure frequency	6.49 (2.06)	6.27 (2.19)	0.20#	0.10 [-0.18, 0.38]
ASMs	1.64 (1.35)	1.77 (1.36)	0.19#	-0.08 [-0.36, 0.19]
Psychometric				
Dissociation	66.28 (20.53)	81.67 (28.27)	>100*	-0.65 [-0.97, -0.34]
Childhood trauma	33.32 (11.35)	39.25 (16.65)	9.82*	-0.47 [-0.78, -0.16]
AEs	37.65 (10.44)	41.78 (9.49)	0.19#	-0.38 [-0.68, -0.08]
Subjective cognition	88.59 (18.77)	80.90 (20.49)	4.47*	0.38 [0.09, 0.67]
Objective cognition	86.78 (10.03)	85.05 (14.54)	0.26#	0.14 [-0.15, 0.43]
Negative affect	0.78 (0.54)	1.05 (0.53)	19.01*	-0.47 [-0.78, -0.17]
Detachment	0.58 (0.45)	0.76 (0.42)	4.07*	-0.38 [-0.69, -0.08]
Antagonism	0.41 (0.37)	0.44 (0.37)	0.18#	-0.06 [-0.35, 0.23]
Disinhibition	0.59 (0.41)	0.82 (0.46)	45.26*	-0.51 [-0.82, -0.21]
Psychoticism	0.42 (0.43)	0.70 (0.51)	>100*	-0.59 [-0.90, -0.29]
Anxiety				
Clinicodemographic				
Age at admission	41.75 (16.44)	35.02 (13.25)	8.73*	0.40 [0.12, 0.68]
Disease duration	13.23 (12.81)	13.38 (13.85)	0.16#	-0.11 [-0.28, 0.26]
Seizure frequency	6.47 (2.07)	6.54 (1.96)	0.16#	-0.03 [-0.31, 0.24]
ASMs	1.83 (1.38)	1.49 (1.22)	0.63	0.23 [-0.04, 0.51]
Psychometric				
Dissociation	69.68 (23.02)	79.91 (29.83)	5.24*	-0.39 [-0.68, -0.10]
Childhood trauma	33.64 (12.35)	39.71 (16.33)	10.67*	-0.43 [-0.73, -0.14]
AEs	30.01 (10.86)	42.93 (11.10)	2.38	-0.34 [-0.63, -0.05]
Subjective cognition	84.97 (19.99)	82.39 (20.23)	0.23#	0.12 [-0.16, 0.40]
Objective cognition	85.96 (11.56)	88.64 (9.37)	0.55	-0.23 [-0.51, 0.05]
Negative affect	0.81 (0.55)	1.04 (0.59)	3.58*	-0.38 [-0.68, -0.08]
Detachment	0.67 (0.51)	0.76 (0.56)	0.30#	-0.16 [-0.46, 0.13]
Antagonism	0.45 (0.40)	0.36 (0.33)	0.46	0.22 [-0.08, 0.52]

Disinhibition	0.65 (0.45)	0.73 (0.42)	0.31#	-0.17 [-0.47, 0.13]
Psychoticism	0.48 (0.46)	0.69 (0.56)	4.85*	-0.40 [-0.71, -0.10]

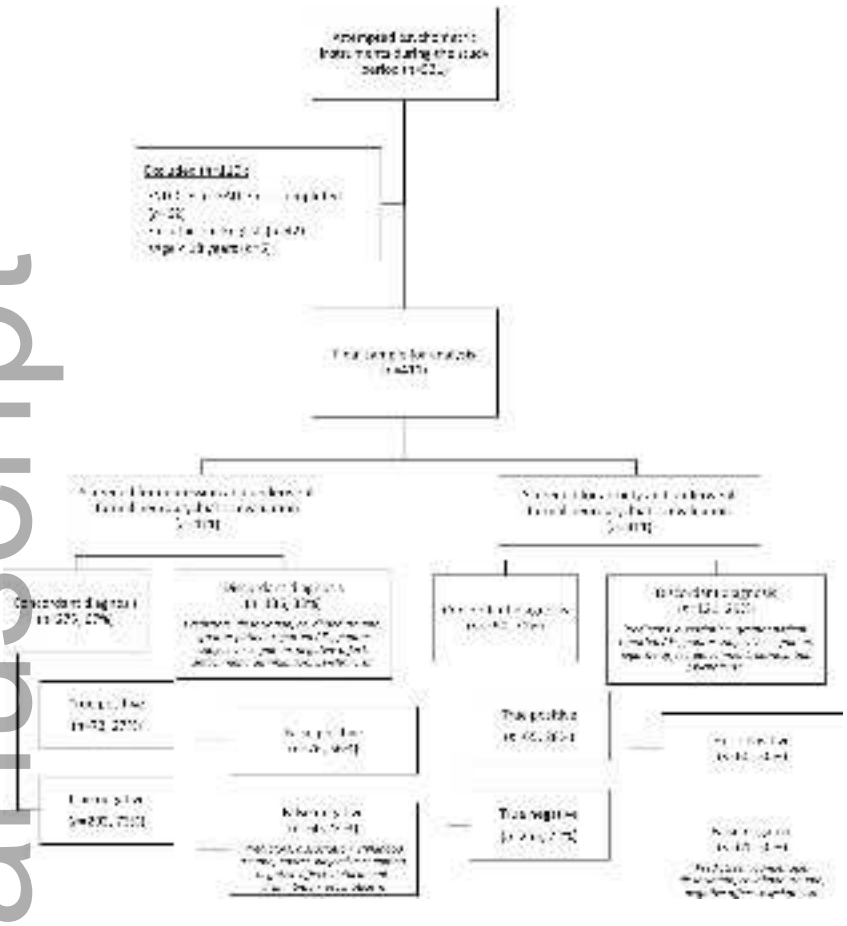
Note: BF_{10} = The Bayes factor for the alternative hypothesis. * indicates $BF_{10} > 3$, which provides support for the alternative hypothesis. # indicates $BF_{10} < 1/3$, which provides support for the null hypothesis. *D* = Cohen's d. *HPDI* = highest posterior density intervals. ASM = antiseizure medication. AEs = patient-reported adverse events.

Table 5. Depression and anxiety false positives vs true positives.

	Mean (SD)			
Variable	*False positive*	*True positive*	*BF_{10}*	*d [95% HPDIs]*
Depression				
Clinicodemographic				
Age at admission	41.26 (15.26)	37.11 (13.86)	0.70	0.26 [-0.05, 0.58]
Disease duration	13.53 (12.41)	13.01 (11.84)	0.18#	0.04 [-0.27, 0.35]
Seizure frequency	6.49 (1.92)	6.43 (2.22)	0.18#	0.03 [-0.28, 0.33]
ASMs	1.63 (1.18)	1.72 (1.41)	0.19#	-0.07 [-0.38, 0.24]
Psychometric				
Dissociation	106.90 (31.66)	106.98 (33.15)	0.19#	0.00 [-0.33, 0.33]
Childhood trauma	44.17 (20.18)	43.91 (17.76)	0.19#	0.01 [-0.33, 0.35]
AEs	54.13 (7.23)	52.80 (7.22)	0.31#	0.17 [-0.16, 0.50]
Subjective cognition	63.43 (19.09)	63.92 (20.66)	0.19#	-0.02 [-0.34, 0.30]
Objective cognition	86.79 (8.01)	84.70 (11.03)	0.38	0.20 [-0.12, 0.52]
Negative affect	1.60 (0.60)	1.56 (0.65)	0.21#	0.06 [-0.28, 0.40]
Detachment	1.38 (0.59)	1.21 (0.65)	0.52	0.25 [-0.10, 0.60]
Antagonism	0.57 (0.46)	0.58 (0.49)	0.20#	-0.01 [-0.36, 0.34]
Disinhibition	1.21 (0.49)	1.10 (0.49)	0.41	0.21 [-0.13, 0.57]
Psychoticism	1.00 (0.49)	1.03 (0.53)	0.21#	-0.07 [-0.41, 0.23]
Anxiety				
Clinicodemographic				
Age at admission	35.88 (14.38)	40.02 (14.08)	0.63	-0.26 [-0.61, 0.07]
Disease duration	10.03 (10.61)	12.43 (14.26)	0.32#	-0.17 [-0.51, 0.16]
Seizure frequency	6.52 (2.03)	6.20 (2.31)	0.26#	0.13 [-0.20, 0.47]

ASMs	1.45 (1.26)	1.53 (1.31)	0.20	-0.06 [-0.40, 0.27]
Psychometric				
Dissociation	107.48 (33.38)	107.34 (33.24)	0.20#	0.00 [-0.35, 0.36]
Childhood trauma	48.73 (20.67)	41.40 (15.96)	126	0.34 [-0.03, 0.72]
AEs	53.23 (8.55)	51.96 (7.45)	0.27#	0.14 [-0.21, 0.50]
Subjective cognition	67.03 (20.63)	61.87 (23.08)	0.41	0.21 [-0.14, 0.57]
Objective cognition	87.17 (8.33)	82.92 (10.08)	2.02	0.42 [-0.07, 0.89]
Negative affect	1.72 (0.59)	1.48 (0.59)	1.47	0.37 [0.00, 0.75]
Detachment	1.18 (0.57)	1.25 (0.67)	0.24#	-0.10 [-0.47, 0.25]
Antagonism	0.50 (0.45)	0.62 (0.47)	0.47	-0.24 [-0.61, 0.13]
Disinhibition	1.14 (0.53)	1.15 (0.52)	0.21#	-0.03 [-0.39, 0.33]
Psychoticism	0.96 (0.54)	1.00 (0.50)	0.22#	-0.06 [-0.43, 0.30]

Note: BF_{10} = The Bayes factor for the alternative hypothesis. * indicates $BF_{10} > 3$, which provides support for the alternative hypothesis. # indicates $BF_{10} < 1/3$, which provides support for the null hypothesis. *d* = Cohen's d. *HPDI* = highest posterior density intervals. ASM = antiseizure medication. AEs = patient-reported adverse events.



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