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Brief Communication

Validation of the Polish version of the Hospital Anxiety and Depression Scale for anxiety disorders in patients with epilepsy

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ABSTRACT

Objective: Anxiety disorders are frequent comorbid disorders in patients with epilepsy (PWEs). The availability of validated screening instruments to detect anxiety disorders in PWEs is limited. The aim of the present study was to validate the Polish version of the Hospital Anxiety and Depression Scale (HADS) in adult PWEs for the detection of anxiety disorders.

Methods: A total of 96 outpatients with epilepsy completed the self-reported symptom scale, the HADS, and were diagnosed using the structured clinical interview for Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR) axis I disorders (SCID-I). The sensitivity, specificity, positive and negative predictive values (PPV and NPV, respectively), and receiver operating characteristic (ROC) curves were assessed to determine the optimal threshold scores for the HADS anxiety subscale (HADS-A).

Results: Receiver operating characteristic analyses showed areas under the curve at 80.8%. For diagnoses of anxiety disorder, the HADS-A demonstrated the best psychometric properties for a cutoff score ≥10 with sensitivity of 81.3%, specificity of 70.0%, PPV of 31.5%, and NPV of 94.9%.

Conclusions: The HADS-A proved to be a valid and reliable psychometric instrument in terms of screening for anxiety disorders in our sample of PWEs. In the epilepsy setting, the HADS-A maintains adequate sensitivity, acceptable specificity, and high NPV but low PPV for diagnosing anxiety disorders with an optimum cutoff score ≥10.

1. Introduction

Epilepsy is one of the world's most prevalent noncommunicable diseases, affecting approximately 50 million people globally. Anxiety disorders are commonly underrecognized psychiatric comorbidities in patients with epilepsy (PWEs) [1]. Comorbid anxiety disorders can have adverse effects on the course and prognosis of epilepsy management, with lower overall health-related quality of life and increased risk of suicidal ideation and suicide attempts [2].

Many recent epidemiological studies have found the prevalence of depression and anxiety to be higher in people with epilepsy than in those without epilepsy, as 9–37% of people with epilepsy have depression and 11–25% have anxiety, which are higher proportions than found in those without epilepsy. There are common pathogenic mechanisms shared by depression, anxiety, and epilepsy. Serotonin, norepinephrine, dopamine, gamma-aminobutyric acid, and glutamate are likely involved in the expression of all three disorders. In depression and anxiety, changes in the noradrenergic and serotonergic systems are implicated as playing significant roles in the expression of these disorders. There appears to be increased noradrenergic activity contrasting with decreased activity in the serotonergic systems. In epilepsy, if there is a decrease in serotonergic or noradrenergic transmission, kindling of seizures occurs, seizure activity increases, and the severity intensifies. Increasing serotonin and noradrenaline transmission helps to prevent seizures, and a reduction will increase the likelihood that a seizure will occur. Thus, the common pathogenic mechanisms shared by depression, anxiety, and epilepsy reveal a neurobiological connection among the disorders. Serotonin, norepinephrine, dopamine, gamma-aminobutyric acid, and glutamate are likely involved in the expression of each disorder. Various brain areas, including the frontal, temporal, and limbic regions, are associated with the biological pathogenesis of depression and anxiety in people with epilepsy. There is evidence of brain changes occurring in the limbic–cortical–striatal–pallidal–thalamic circuit in both anxiety and depression. These structures include the frontal cortex, hippocampus, thalamus, amygdala, putamen, caudate, and basal ganglia. A complete correspondence between structural impairment in the limbic–cortical–striatal–pallidal–thalamic circuit and resulting depression and anxiety is not confirmed. It is likely

Abbreviations: AUC, area under the curve; DSM-IV-TR, Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision; HADS, Hospital Anxiety and Depression Scale; ICD-10, International Statistical Classification of Diseases and Related Health Problems, 10th Revision; N/A, not available; SCID-I, structured clinical interview for DSM-IV-TR axis I disorders.

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that a structural impairment in this circuit results in an increased vulnerability to depression and anxiety. Depression is associated with increased bilateral amygdala volumes and hypometabolism in the frontal regions and in the temporal lobes. Anxiety is associated with larger mean amygdala volumes. These imaging studies provide further support for the notion that depression, anxiety, and epilepsy have a neurobiological link [3].

The availability of well-validated, self-reported screening psychometric instruments to detect anxiety disorders in PWEs is limited. A self-reported psychometric instrument for screening purposes should be well-validated with optimized cutoff points for the targeted population set against the "gold standard," such as standardized structured psychiatric interviews to produce psychiatric diagnoses. The consensus statement highlights the importance of screening for anxiety in PWEs, recommending the Hospital Anxiety and Depression Scale (HADS) as a screening instrument [4,5]. The HADS was developed as a tool to identify anxiety and depressive disorders in nonpsychiatric patients within a hospital setting and was broadly used in populations with diverse somatic illnesses [6]. Versions are available in several languages, including Polish [7]. The HADS is a self-reported scale with no items related to somatic symptoms. It minimizes the occurrence of false positives in PWEs who are screened for anxiety disorders [6]. To date, there have been only two validation studies in PWEs regarding anxiety disorders; employing the standard English version of the HADS [5] and the Arabic language version of the scale [8], they produced some confounding results.

The aim of this study was to validate the psychometric properties of the Polish version of the HADS anxiety subscale in PWEs in order to determine its optimal specificity, sensitivity, and cutoff scores for identifying depressive disorders.

2. Methods

2.1. Study population

This study used data collected as part of a larger study reported elsewhere [1]. Briefly, 118 consecutive PWEs from a tertiary epilepsy center were screened, with 96 patients enrolled. Subjects who received a diagnosis of active epilepsy according to the International League Against Epilepsy criteria [9] receiving stable antiepileptic treatment in the prior 2 months and aged 18–65 were included. The exclusion criteria selected to reduce the impact of periictal and ictal psychiatric symptoms were last seizure within 24 h of examination and more than 10 seizures in the prior month. Exclusion criteria also included a history of severe traumatic brain injury with midline shift as determined by neuroimaging, neurosurgery, the presence of an uncontrolled disease, or serious neurological disorder. Further exclusion criteria were the identification of psychogenic nonepileptic seizures (pseudoseizures) with no evidence of epilepsy as identified with video electroencephalography, mental retardation, alcohol and/or drug dependence or abuse in the past 6 months, and borderline antisocial personality disorder as determined by psychiatric interview, as the psychiatric symptomatology manifested in these psychopathologic domains may confound estimates of morbidity rates across anxiety disorders.

This study was conducted in agreement with the Declaration of Helsinki following the approval of the ethical research committee of the institution. Written informed consent was obtained from each study participant.

2.2. Evaluation

All the subjects were assessed at a single study visit by the same investigator (MSW) and diagnosed using the structured clinical interview for Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision (DSM-IV-TR) axis I disorders (SCID-I) [10]. The structured interview was used to obtain information on the disease history and sociodemographic status of the patients, including their gender, age, economic situation, marital status, age of seizure onset, duration of epilepsy, seizure frequency, seizure type, experience of auras and duration of treatment, existence of lesions, and psychiatric history. Computed tomography/magnetic resonance imaging, electroencephalogram, and laboratory tests results were available for the majority of the subjects. The data were corroborated by referral source records from the epileptologist.

The HADS was developed to identify the caseness of anxiety disorders and depression among patients in nonpsychiatric hospital settings. The tool includes 14 items, seven related to anxiety (HADS anxiety subscale (HADS-A)) and seven related to depression (HADS depression subscale (HADS-D)), each scored between 0 and 3. The HADS-A assesses features of a generalized anxiety state, such as restlessness, panic attacks, and anxious thoughts and mood. For analyses, the patients were assigned to a comprehensive diagnostic group of anxiety disorders including subjects with panic disorder, generalized anxiety disorder, and agoraphobia. The recommended score of ≥8 on an individual scale should be regarded as a possible case and ≥11 as a definite case [6].

2.3. Statistics

In order to determine the diagnostic sensitivity and specificity of the HADS for the DSM-IV anxiety disorder diagnoses and determine an optimal cutoff point, a receiver operator characteristic (ROC) curve was obtained for the HADS-A.

The area under the curve (AUC) values were interpreted according to the following guidelines: 0.9–1, excellent; 0.8–0.9, good; 0.7–0.8, fair; and 0.6–0.7, poor. Cutoff values were established with the (0, 1) minimum distance method giving equal weight to sensitivity and specificity. There were no missing data or outliers. The anxiety disorders subgroup and the subgroup without anxiety disorders were compared with respect to sex, age, education, family, and socioeconomic and epilepsy-related factors. Drug-resistant epilepsy defined as two consecutive failures of properly selected and applied and tolerated by the patient's antiepileptic treatments in mono- or polytherapy [11] was found in 73% of the subjects.

The frequencies and descriptive statistics were analyzed for each variable. Comparisons between the patients with current anxiety disorder and those without anxiety disorder were made using Student's *t*-tests for normally distributed continuous data, Mann–Whitney's U-test for nonnormally distributed data, and Fisher's exact test for categorical data. A value of $p < 0.05$ was considered statistically significant.

Table 1
Demographic and clinical characteristics of study population. (Modified from [1]).

	N = 96 (%)
Male sex (%)	31 (32.3)
Age, in years (SD)	36.6 (12.0)
Age of seizure onset (SD)	19.5 (11.6)
Duration of epilepsy (SD)	17.0 (11.8)
Number of seizures/last month — median (IQR)	3 (2.5)
Seizure type (%)	
Generalized	15 (15.6)
Simple partial	7 (7.3)
Complex partial	27 (28.1)
Partial evolving to general	47 (49.0)
Tonic–clonic	10 (10.4)
Absence	2 (1.0)
Myoclonic	1(1.0)
Atonic	2 (2.1)
Number of AEDs (IQR)	2 (1.2)

SD — standard deviation.
IQR — interquartile range.