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Reliability and validity of the Chinese version of the Patient Health Questionnaire 9 (C-PHQ-9) in patients with epilepsy

Nian-ge Xia [a,1], Jia-he Lin [a,1], Si-qi Ding [a], Fei-rong Dong [b], Jing-zan Shen [a], Yan-ru Du [a], Xin-shi Wang [a], Yan-yan Chen [a], Zhen-guo Zhu [a], Rong-yuan Zheng [a], Hui-qin Xu [a,*]

[a] Department of Neurology, the First Affiliated Hospital of Wenzhou Medical University, Wenzhou 325000, Zhejiang Province, China
[b] Department of Psychiatry, the First Affiliated Hospital of Wenzhou Medical University, Wenzhou 325000, Zhejiang Province, China

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ABSTRACT

Objective: The aim of this study was to evaluate the clinical reliability and validity of the Chinese version of the Patient Health Questionnaire 9 (C-PHQ-9) in patients with epilepsy.
Methods: A total of 213 consecutive adult patients with epilepsy were evaluated. Receiver operating characteristic (ROC) analysis was performed using C-PHQ-9 and Chinese version of Patient Health Questionnaire 2 (C-PHQ-2) as predictors and the Mini International Neuropsychiatric Interview Plus Version 5.0.0 as the gold standard.
Results: The C-PHQ-9 was easily understood and quickly finished by the patients. According to the gold standard, the prevalence of current major depressive disorder in this population was 16.4%. Cronbach's α coefficient for the C-PHQ-9 was 0.860. The ROC analysis showed an area under the curve (AUC) of 0.888 (95% confidence interval [CI] = 0.838–0.927). At a cutoff score of >6, the C-PHQ-9 had a sensitivity of 82.86%, a specificity of 84.27%, a positive predictive value of 50.9%, and a negative predictive value of 96.2%. The C-PHQ-2 at a cutoff score of >1 resulted in the greatest balance of sensitivity and specificity (77.14% and 75.28%, respectively).
Conclusion: Our findings support a high reliability and validity for the C-PHQ-9 as a screening tool for the detection of current major depression in Chinese patients with epilepsy.

1. Introduction

Depression is the most common psychiatric comorbidity in patients with epilepsy (PWE) [1], with a reported prevalence of 22.9% and 23.1%, respectively, according to two recent meta-analyses [2,3]. Depression can have negative effects on quality of life [4], reduce medication compliance [5], and even increase the risk of suicide [6,7] in those with epilepsy. Despite the high prevalence of depression in PWE, they remain underreported, underdiagnosed, and undertreated. Therefore, promptly identifying and timely treating depression plays an important role in the improvement of the overall health outcomes of PWE.

Many methods are available to detect depression, including psychiatric or psychological assessments, structured or semistructured interviews, and self-report screening tools [8]. Fully structured and semistructured interviews, such as the Structured Clinical Interview for the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM–IV) (SCID) and the Mini International Neuropsychiatric Interview (MINI), are designed for use by well-trained clinicians but may be inconvenient and time-consuming for use in practice. However, self-report screening tools may be more effective in assessing depressive symptoms because they are often brief, standardized, and free or inexpensive [8]. A limited number of clinical self-report screening instruments for depression, such as the Neurological Disorder Depression Inventory for Epilepsy (NDDI-E) [9,10], the Beck Depression Inventory-II (BDI-II) [11,12], and the Hospital Anxiety and Depression Scale (HADS) [11,13,14], have already been validated in PWE. The Patient Health Questionnaire 9 (PHQ-9) is also a depression-screening tool and has been developed for use in the general population. Its diagnostic validity was confirmed in more than 11,000 patients, most of whom came from primary care clinics [15]. As far as we know, there have been only two validation studies conducted with the standard English version of the PHQ-9 in PWE regarding depression disorders [16,17]. The present study aimed to evaluate the clinical reliability and validity of the Chinese version of the PHQ-9 (C-PHQ-9) in Chinese PWE.

2. Methods

2.1. Participants

A total of 213 Chinese outpatients were recruited from the specialized epilepsy clinic of the First Affiliated Hospital of Wenzhou Medical

* Corresponding author at: Department of Neurology, The First Affiliated Hospital of Wenzhou Medical University, Wenzhou 325000, Zhejiang Province, China.
E-mail address: xuhuiqin@wmu.edu.cn (H. Xu).
[1] The first two authors contributed equally to this paper.

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University, China, between January and December 2018. Inclusion criteria were as described in our previous publication [18]: (1) confirmed diagnosis of epilepsy according to the International League Against Epilepsy (ILAE) criteria, (2) patients greater than or equal to 18 years old, (3) Chinese native speaker and fluency in Putonghua, and (4) willingness to participate and provide written informed consent. The exclusion criteria were as follows: (1) suffering from other severe psychiatric disorders such as mental retardation or alcohol or drug dependence, (2) a diagnosis of antisocial or schizotypal personality disorder, or (3) unable to understand or complete the questionnaires. Each participant was examined first by a neurologist (JHL) who was trained in the application of the C-PHQ-9 and then assessed using the Chinese version of the MINI (C-MINI) by a well-trained psychiatrist (FRD) within one day.

Patient details including sex, age, age at onset, course of epilepsy, marital status, occupational status, duration of education, type of seizures, and the number of antiepileptic drugs (AEDs) were collected from Wenzhou Epilepsy Follow-Up Registry Database (WEFURD), which were introduced in a previous publication [19]. The study was approved by the Ethics Committee of the First Affiliated Hospital of Wenzhou Medical University, and all participants signed a written informed consent form for participation in the study.

2.2. Instruments

2.2.1. The Chinese version of the Mini International Neuropsychiatric Interview (C-MINI) 5.0.0

The MINI is a brief, structured diagnostic interview that uses the classical DSM-IV and the International Statistical Classification of Diseases and Related Health Problems 10th Revision (ICD-10) criteria to diagnose depression [20]. The MINI has been translated into different versions and proved to be effective and reliable in clinical research and clinic application [21–24], including the Chinese version of the MINI in 2009 [25]. The Chinese version of the MINI Plus version 5.0.0 was administered and is considered to be the gold standard for the diagnosis of major depressive disorder (MDD) in this study.

2.2.2. The Chinese version of Patient Health Questionnaire 9 (C-PHQ-9) and of the Patient Health Questionnaire 2 (C-PHQ-2)

The PHQ-9 is a 9-item self-report instrument used to assess depressive symptoms over the past 2 weeks. The nine items pertain to the DSM [26] criteria for MDD: (1) anhedonia; (2) depressed mood; (3) trouble sleeping; (4) feeling tired; (5) change in appetite; (6) guilt, self-blame, or worthlessness; (7) trouble concentrating; (8) feeling slowed down or restless; and (9) thoughts of being better off dead or hurting oneself. All 9 items are scored from 0 to 3, and the total scores range from 0 to 27. As a severity measure in the general population, scores of 0 to 4 indicate no depression, scores of 5 to 9 indicate mild depression, scores of 10 to 14 indicate moderate depression, scores of 15 to 19 indicate moderately severe depression, and scores of 20 to 27 indicate severe depression [8]. Fiest and colleagues validated the PHQ-9 and showed a cutoff score of 9 for screening current major depressive disorder [16], while Rathore and colleagues' study indicated a different cutoff score of 10 [17]. The C-PHQ-9 has also been validated and widely applied in the detection of depression in Chinese general populations [27].

The PHQ-2, consisting of the first two items (two cardinal symptoms of depression: anhedonia and depressed mood) of the PHQ-9, is also considered a screening tool for assessing depression. Both items are scored from 0 to 3, and the total scores range from 0 to 6.

2.3. Statistical analysis

Statistical analyses were performed using SPSS version 17.0 (SPSS Inc., Chicago, IL, USA) and MedCalc 18.2 (MedCalc Software, Ostend, Belgium). The frequencies and descriptive statistics were analyzed for each variable. Categorical demographic and clinical variables were compared using the chi-square test or Fisher's exact test. Continuous demographic and clinical variables were compared by the nonparametric Mann–Whitney *U* test. A two-tailed p-value below 0.05 was adopted as the statistical significance level for all tests. Cronbach's α coefficient was used to measure the internal consistency of the C-PHQ-9.

Empirical receiver operating characteristic (ROC) curves were generated using the MINI-Plus diagnosis of depression as the gold standard and C-PHQ-9 and Chinese version of Patient Health Questionnaire 2 (C-PHQ-2) scores as predictors. The sensitivity, specificity, and positive and negative predictive values at possible cutoff points were calculated. The area under the curve (AUC) and 95% confidence intervals (CIs) of the ROC curve were also calculated.

3. Results

3.1. Clinical and demographic characteristics in patients with epilepsy

Two hundred thirteen patients were finally evaluated in the epilepsy clinic during the data collection period. Thirty-five were found to have major depressive disorder according to the MINI, with an estimated prevalence of 16.4%. The demographic and clinical characteristics of the PWE are shown in Table 1. The sample consisted of 46.5% males; the mean age of the patients was 33.17 years; 62.9% were married; their mean length of education was 11.32 years, and 63.8% were employed.

3.2. Evaluation of the C-PHQ-9 and C-PHQ-2

The C-PHQ-9 was easily comprehended by all patients, and every patient completed the test within 5 min. The Cronbach's α coefficient for the C-PHQ-9 was 0.860, which shows excellent internal consistency and reliability. As shown in Table 2, all C-PHQ-9 items were significantly and positively associated with the total C-PHQ-9 score, and none of these items would have significantly increased the α coefficient if deleted.

Table 1
Demographic and clinical characteristics of the patients with epilepsy.

Characteristic	Overall (N = 213)	
	With depression (N = 35)	Without depression (N = 178)
Male(%)	51.4	45.5
Average age (years)(range)	37.8(18–74)	32.3(18–67)
Age at onset(years) (range)	21.8(2–57)	21.3(0–67)
Course (years) (range)	15.8(1–47)	10.9(0–48)
Marital status		
Unmarried/Single(%)	25.7	33.3
Married(%)	71.4	61.0
Divorced(%)	2.9	5.6
Duration of education (years) (SD)	10.4(4.2)	11.5(3.8)
Occupational status		
Employed(%)	42.9	68.0
Unemployed(%)	31.4	21.9
Retired(%)	8.6	2.8
Student(%)	17.1	7.3
Seizure type		
Simple partial seizure(%)	8.6	3.9
Complex partial seizure(%)	31.4	28.7
Secondarily generalized seizure(%)	45.7	51.7
Tonic–clonic seizure(%)	5.7	10.7
Absence seizure(%)	5.7	5.1
Myoclonic seizure(%)	2.9	0
Number of AEDs		
None(%)	5.7	1.7
Monotherapy(%)	22.9	51.1
Dual therapy(%)	65.7	41.0
Polytherapy (≥3) (%)	5.7	6.2
Currently taking antidepressants(%)	22.9	6.7

SD = standard deviation

Table 2
Corrected item–total correlations and Cronbach's α if the item is deleted from the C-PHQ-9.

Item	Corrected item—total correlation	Cronbach's alpha if item is delete
1	0.649	0.839
2	0.694	0.835
3	0.493	0.858
4	0.665	0.837
5	0.504	0.852
6	0.733	0.829
7	0.545	0.849
8	0.553	0.848
9	0.504	0.854

Figs. 1 and 2 display ROC curves generated for depression diagnosed by the MINI-Plus as the gold standard and the C-PHQ-9 and C-PHQ-2 scores as predictors. The optimal cutoff point for the curve is highlighted, as determined by the Youden index and the point closest to the upper left corner. For the C-PHQ-9, a cutoff score of >6 led to a sensitivity of 82.86% and specificity of 84.27%. For the C-PHQ-2, a cutoff score of >1 led to a sensitivity of 77.14% and specificity of 75.28%. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV), and AUC are presented in Table 3. At a cutoff score of >6, the C-PHQ-9 showed an acceptable PPV of approximately 50% and an excellent NPV of 96.2%. The ROC analysis showed an AUC of 0.888 (95%CI = 0.838–0.927) for C-PHQ-9 and an AUC of 0.802 (95%CI = 0.742–0.853) for C-PHQ-2. Both C-PHQ-9 and C-PHQ-2 had an AUC significantly greater than 0.5 (both $p < 0.0001$). However, the AUC for the C-PHQ-9 was significantly larger than the AUC for the C-PHQ-2 ($p = 0.0079$) in pairwise comparisons. Thus, there was a tendency for the C-PHQ-9 to diagnose depressive symptoms better than the C-PHQ-2 was able to.

4. Discussion

The main purpose of our study was to investigate the validity and reliability of the C-PHQ-9 for depression in Chinese PWE. To make an effective diagnosis, we used the complete version of the MINI-Plus 5.0.0 as a reference standard in psychiatric research. In our study, a cutoff score of 6 or greater on the C-PHQ-9 is appropriate when screening for current major depression in PWE, maintaining the best balance between sensitivity and specificity (82.86% and 84.27%, respectively). At this cutoff, the AUC was 0.888, which presented a high level of diagnostic accuracy compared with the reference standard. Furthermore, Cronbach's α coefficient value of 0.860 indicates acceptable levels of internal consistency and reliability for the C-PHQ-9. Taken together, these findings confirm the validity and reliability of the C-PHQ-9 as a major screening tool for depressive disorder in PWE.

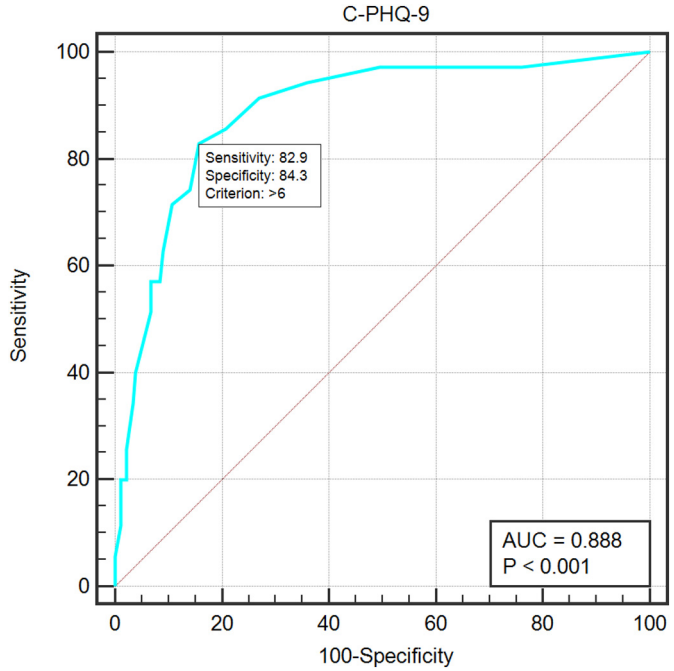

Fig. 1. Receiver operating characteristic curve of the C-PHQ-9.

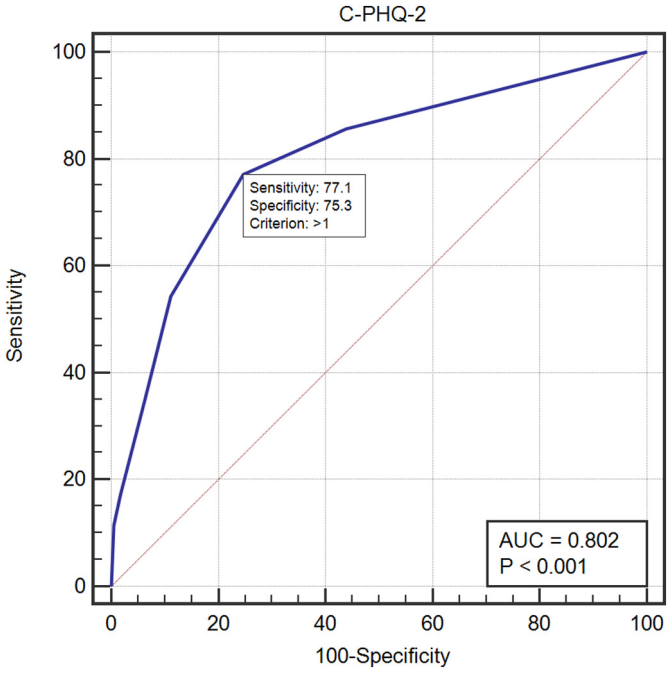

Fig. 2. Receiver operating characteristic curve of the C-PHQ-2.

To date, there have been only two validation studies for the PHQ-9 assessed as a screening tool in epilepsy [16,17]. Fiest et al. [16] evaluated three depression-screening tools (HADS, the PHQ-2, and the PHQ-9, in 300 persons with epilepsy compared with the SCID). The PHQ-9 at a cutoff point of 9 had the optimal balance of sensitivity (82.6%) and specificity (82.2%) with an AUC of 88% (PPV 44.2% and NPV 96.8%). The current study first established firm validity for the C-PHQ-9 as a screening tool for depression disorders in PWE, emphasizing its reliability in a tertiary-care program. Rathore et al. [17] validated the PHQ-9 in 172 PWE compared with the MINI interview. The PHQ-9 demonstrated the best psychometric properties for a cutoff score of 10 with a sensitivity of 0.92, a specificity of 0.74, an AUC of 0.914, a PPV of 0.46, and an NPV of 0.97. Both studies gave similar results for an optimal cutoff score and the accuracy of the scale. According to the results of the present study, we find that the C-PHQ-9 could also produce similarly stable and predictable results in PWE. However, the optimal cutoff scores (>6) in our study are lower than the recommended thresholds suggested in these two previous studies (9 and 10, respectively). The disparities between the studies may be due to the differences in social culture and language [28]. Moreover, not all of the previous studies used the MINI for detecting depression; therefore, variation in the reference standards used may result in different thresholds for the PHQ-9.

Once the psychometric properties and validity of the PHQ-9 were established, we also compared the PHQ-2 with the PHQ-9 to assess its validity for depression screening. A previous study found high sensitivity and PPV for the PHQ-2 (80% and 100%, respectively) in PWE using the MINI as the reference standard [29]. The present study, however, found a PPV of 38.0% and sensitivity of 77.14% at the optimal cutoff using the C-PHQ-2. In pairwise comparisons, the AUC for the C-PHQ-2

Table 3
Statistics and selected coordinates of the ROC curves generated using the Chinese version of the PHQ-9 and PHQ-2 scores as predictors and MINI-Plus 5.0.0 diagnosis of depression as gold standard in patients with epilepsy.

Scales and cutoff point	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	AUC	SE	95% CI	p-Value
C-PHQ-9								
>5	85.71	79.21	44.8	96.6				
>6[a]	82.86	84.27	50.9	96.2	0.888	0.0309	0.838–0.927	<0.0001
>7	74.29	85.96	51.0	94.4				
>9	62.86	91.01	57.9	92.6				
>10	57.14	91.57	57.1	91.6				
C-PHQ-2								
>1[a]	77.14	75.28	38.0	94.4	0.802	0.0425	0.742–0.853	<0.0001
>2	54.29	88.76	48.7	90.8				
>3	34.29	93.82	52.2	87.9				

Abbreviations: PPV = positive predictive value; NPV = negative predictive value; AUC = area under the curve; SE, standard error; CI, confidence interval; ROC = receiver operating characteristic.
[a] Cutoff point indicated by the Youden index.

was significantly smaller than the AUC for the C-PHQ-9. Thus, the C-PHQ-2 is not recommended to screen for depression in PWE, which is similar to the result from a previous study [16].

Although the PHQ-9 is brief, self-administered, and widely used in various clinical settings as a screening instrument, it is not routinely used for detecting depressive disorders in PWE. Kanner et al. stated that the PHQ-9 may be invalid in PWE because the somatic symptoms of depressive disorders could overlap with common adverse effects of antiepileptic medications [30]. Specifically, attention loss, fatigue, and sleep difficulties may also result from medications [8]. However, the PHQ-9 presented good sensitivity and specificity for the detection of depression in PWE in our study and the previous two studies. Thus, the PHQ-9 is an appropriate and useful screening instrument for depression in epilepsy, although further validated studies from different cultures and languages are needed.

The present study makes new contributions to our further understanding of the C-PHQ-9; however, several possible limitations must be discussed. First, all participants of the study came from the specialized epilepsy clinic of a tertiary hospital, which may limit the generalizability of the results to other patients with different severities or from different regions. Future studies targeting different demographic and regional populations with epilepsy should be explored. Second, the cross-sectional study design could have affected the results. Finally, we should realize that although self-report screening questionnaires are effective and helpful tools in quantifying depressive symptoms in persons with epilepsy, they are not a replacement for a comprehensive psychiatric evaluation.

In conclusion, our results support the notion that the C-PHQ-9 is a suitable screening tool for depression in Chinese PWE. The C-PHQ-9 score is a valid indicator of depressive symptoms in PWE and possesses adequate sensitivity and specificity, acceptable PPV, and high NPV with an optimal cutoff score of >6 for depression diagnosis.

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Conflict of interest

The authors declare no conflict of interest.

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