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Validation of the Generalized Anxiety Disorder-7 (GAD-7) among Chinese people with epilepsy

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ABSTRACT

Objective: To validate the Chinese version of the Generalized Anxiety Disorder-7 (GAD-7) in Chinese people with epilepsy (PWE).
Methods: A consecutive cohort of PWE from the West China Hospital was recruited. Each patient received a psychiatric evaluation comprising the Mini International Neuropsychiatric Interview (MINI) and the GAD-7. Demographic and clinical characteristics were collected. Cronbach's α coefficient was calculated and receiver operating curve (ROC) analysis was conducted.
Results: A total of 213 PWE completed the psychiatric evaluation. The GAD-7 was easily understood and quickly completed by all participants. Fifty patients (23.5%) had GAD according to the MINI criteria. Cronbach's α coefficient for the GAD-7 was 0.888. ROC analysis showed an area under the curve of 0.974 (95% CI = 0.956–0.993). At a cut-off score of >6, the GAD-7 achieved the largest Youden index of 0.854 with a sensitivity of 94%, a specificity of 91.4%, a positive predictive value of 77% and a negative predictive value of 98%.
Significance: The Chinese version of the GAD-7 is a valuable tool for screening for GAD in Chinese PWE.

1. Introduction

Many epidemiological studies have found the prevalence of depression and anxiety to be higher in people with epilepsy (PWE) than in those without epilepsy (Kwon and Park, 2014). Comorbid anxiety in PWE has been highlighted because of its negative impact on quality of life (QOL), which has been shown to be equal to that of depression (Johnson et al., 2004; Kanner et al., 2010; Kwon and Park, 2013). The prevalence of anxiety in adult PWE ranges from 11% to 50%, depending on the population investigated and the anxiety measure instrument used (Munger Clary, 2014). Comorbid anxiety is associated with more side effects of antiepileptic drugs (AEDs) (Kanner et al., 2012), greater cognitive difficulties (Velissaris et al., 2009), poorer seizure outcome (Kanner et al., 2009; Petrovski et al., 2010), higher risk of suicide (Gandy et al., 2013), increased rate of hospital admission and heavier economic burden (Hamilton et al., 2014; Noble et al., 2012). Indeed anxiety was found to be the most important predictor of QOL in some studies (Huang et al., 2011; Kwan et al., 2009). Furthermore, comorbid occurrence of mixed depressive/anxiety disorders yielded an even greater negative impact on QOL than did anxiety disorders alone (Kanner et al., 2010; Kwon and Park, 2013).

Early detection and appropriate management of depression and anxiety in PWE is crucial for achieving better QOL. From this perspective, the Neurological Disorders Depression Inventory for Epilepsy (NDDI-E) (Gilliam et al., 2006) including its Chinese version (C-NDDI-E) (Tong et al., 2015) have been developed and proven to be valid screening tools for detecting major depressive disorder (MDD) in PWE. The Generalized Anxiety Disorder-7 (GAD-7) has been used as a screening tool for generalized anxiety disorder (GAD) in primary care patients (Kroenke et al., 2007; Spitzer et al., 2006). A score of >9 is considered indicative of likely presence of GAD. It was also suggested as a suitable screening tool for PWE, because it did not have items with somatic symptoms that could be confused with adverse effects of antiepileptic drugs (AEDs), or cognitive symptoms of the seizure disorder or underlying neurologic disorder associated with the epilepsy (Kanner, 2011). Recently, validation of the GAD-7 in PWE was performed in Korea (Seo et al., 2014). It was found that a score of >6 represented GAD in Korean

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PWE, this cut-off score being much lower than that found in studies of primary care patients. The authors explained the gap between the scores as possibly reflecting different composition of the groups of subjects (for example the proportion of men and women being different in the two studies); or ethnic and language differences between the different populations studied. For those reasons, they recommended that further validation studies for GAD-7 should be performed with respect to different disease categories and native languages.

The GAD-7 has been translated into Chinese and validated in general hospital outpatients, with a cut-off score of >9 (He et al., 2010). However, we cannot presume that this cut-off score is likely to be same in Chinese PWE. The aim of the study is to validate the GAD-7 in Chinese PWE.

2. Method

2.1. Participants

Participants were consecutively recruited from the epilepsy outpatient clinic of West China Hospital from March to May 2015. To be enrolled, they had to be ≥18 years old and currently diagnosed with epilepsy according to the International League Against Epilepsy (ILAE) criteria (Fisher et al., 2014). Second, they should be Chinese citizens and had to have received at least primary education so that they could properly understand the questionnaire and interview. Patients with psychogenic non-epileptic seizures or other significant neurological/psychiatric disorders, such as cognitive deficits, aphasia or schizophrenia, which might hamper appropriate understanding and completion of the questionnaire, were excluded. All patients gave written informed consent to state their willingness to participate.

The study protocol and informed consent were approved by the ethics committee of West China Hospital, Sichuan University.

2.2. Psychiatric evaluation and the instruments used

Each patient underwent psychiatric evaluation conducted by a qualified psychiatrist using the following instruments:

2.2.1. Mini International Neuropsychiatric Interview (MINI)

The MINI is an internationally validated structured interview tested to be simple, effective and reliable. It is mainly used for screening and diagnosis of 16 axis I psychiatric disorders and one personality disorder in DSM-IV and ICD-10 (Sheehan et al., 1998). Only the module for GAD of the MINI (Chinese version 5.0.0) was administered. In the current study it was the gold standard for diagnosis of current GAD.

2.2.2. Chinese version of the Generalized Anxiety Disorder-7 (GAD-7)

Spitzer et al. (2006) published the GAD-7 and proved it to be a valid and efficient tool for screening for GAD and assessing its severity. It was a seven-item self-rating instrument. Each item described one of the typical symptoms of GAD and was evaluated by the frequency in which that symptom emerged over the last two weeks: "Not at all" scored zero, "Several days" scored one, "More than half the days" scored two, and "Nearly every day" scored three. In 2010, the GAD-7 was translated into a Chinese version and validated in general hospital outpatients (He et al., 2010). In this study population the Chinese version, as the original GAD-7 study, adopts >9 as the cut-off score.

2.3. Statistical analysis

Statistical analysis was performed with SPSS Version 19.0 (SPSS Inc., Chicago, IL, USA). Categorical demographic and clinical variables were analyzed by Chi-square test or Fisher's exact test, and continuous variables were analyzed by Mann–Whitney U test. A significance level was set at $p < 0.05$ (two-tailed). Internal consistency was analyzed by Cronbach's α coefficient. Receiver operating curves (ROC) analysis was carried out to measure sensitivity, specificity, positive predictive values (PPVs), and negative predictive values (NPVs) for a range of cut-off scores of the GAD-7, with respect to the diagnoses of GAD by the MINI. The ideal cut-off score was settled by the largest Youden index.

3. Results

Two hundred and thirteen PWE completed the psychiatric evaluation and 50 (23.5%) had current GAD according to the MINI. The GAD-7 was fairly easy to understand and complete for the patients. No major difficulties were reported in the process of answering the questionnaire and no items of the scale were left blank.

3.1. Demographic and clinical characteristics

The mean age was 29.86 ± 11.9 years old. There were 109 (51.2%) males and 104 (48.8%) females. In those 50 patients diagnosed as having GAD, gender was equally distributed. Two thirds of them lived in urban areas; 102 (47.9%) were married and 98 were single including the one widowed and two divorced patients who were classified as "unmarried". There was no statistical difference in education level and employment status between the groups with and without GAD. There were more patients with complex partial seizures diagnosed with GAD ($p = 0.046$), while for other seizure types no such difference was found. Patients with idiopathic epilepsy had less GAD ($p = 0.013$). For the GAD group, their seizures occurred more frequently ($p = 0.001$) and more recently ($p = 0.013$), and they were also more likely to be taking multiple AEDs ($p = 0.042$). However, no particular kind of AED was found to be associated with higher anxiety levels. The age at seizure onset and course of disease did not differ between patients with and without GAD. For details see Table 1.

3.2. Patients' response to the GAD-7 and Cronbach's alpha coefficient

The mean GAD-7 score was 4.86 for all the participants. The patients with GAD scored 11.46 in average, far higher than 2.83 scored by those without GAD ($p < 0.001$). For patients who were seizure free in the last six months ($n = 61$), their mean GAD-7 score was 3.75 (±3.8, range 0–15), lower than patients with uncontrolled seizures ($n = 152$) scored (5.30 ± 5.1, range 0–21) ($p = 0.035$). While the seven items responded in different frequencies as Table 2 demonstrates, the GAD-7 had a Cronbach's α coefficient of 0.888 and this coefficient would decrease if any item were deleted. Such details were displayed in Table 3 with corrected item–total correlations for each item.

3.3. ROC curve analysis

As Table 4 and Fig. 1 showed, ROC analysis showed an area under the curve (AUC) of 0.974 (95%CI = 0.956–0.993). A cut-off score of >6, maximizing the Youden Index, yielded a sensitivity of 94%, a specificity of 91.4%, a PPV of 77% and a NPV of 98%.