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Rapid detection of generalized anxiety disorder and major depression in epilepsy: Validation of the GAD-7 as a complementary tool to the NDDI-E in a French sample

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ABSTRACT

Objective: Generalized anxiety disorder (GAD) in people with epilepsy (PWE) is underdiagnosed and undertreated. The GAD-7 is a screening questionnaire to detect GAD. However, the usefulness of the GAD-7 as a screening tool in PWE remains to be validated. Thus, we aimed to: (1) validate the GAD-7 in French PWE and (2) assess its complementarity with regard to the previously validated screening tool for depression, the Neurological Disorders Depression Inventory for Epilepsy (NDDI-E).
Methods: This study was performed under the auspices of the ILAE Commission on Neuropsychiatry. People with epilepsy > 18 years of age were recruited from the specialist epilepsy unit in Marseille, France. The Mini-International Neuropsychiatric Interview (MINI) was performed as gold standard, and the Penn State Worry Questionnaire (PSWQ) and the NDDI-E were performed for external validity. Data were compared between PWE with/without GAD using Chi^2 test and Student's t-test. Internal structural validity, external validity, and receiver operator characteristics were analyzed. A principal component factor analysis with Varimax rotation was performed on the 13 items of the GAD-7 (7 items) plus the NDDI-E (6 items).
Results: Testing was performed on 145 PWE: mean age = 39.38 years old (SD = 14.01, range: 18–75); 63.4% (92) women; 75.9% with focal epilepsy. Using the MINI, 49 (33.8%) patients had current GAD. Cronbach's alpha coefficient was 0.898, indicating satisfactory internal consistency. Correlation between GAD-7 and the PSQW scores was high ($r(145) = .549$, $P < .0001$), indicating good external validity. Factor analysis shows that the anxiety investigated with the GAD-7 and depression investigated with the NDDI-E reflect distinct factors. Receiver operator characteristic analysis showed area under the curve of 0.899 (95% CI 0.838–0.943, $P < 0.0001$) indicating good capacity of the GAD-7 to detect GAD (defined by MINI). Cutoff for maximal sensitivity and specificity was 7. Mean GAD-7 score in PWE with GAD was 13.22 (SD = 3.99), and that without GAD was 5.17 (SD = 4.66).
Significance: This study validates the French language version of the GAD-7 screening tool for generalized anxiety in PWE, with a cutoff score of 7/21 for GAD, and also confirms that the GAD-7 is a short and easily administered test. Factor analysis shows that the GAD-7 (screening for generalized anxiety disorder) and the NDDI-E (screening for major depression) provide complementary information. The routine use of both GAD-7 and NDDI-E should be considered in clinical evaluation of patients with epilepsy.

1. Introduction

Psychiatric disorders are frequent comorbidities in people with epilepsy (PWE) [1], major depressive episode (MDE) and generalized anxiety disorder (GAD) being the two most prevalent [2–5]. The presence of MDE and/or GAD is associated with higher seizure frequency [6–8], more adverse effects of antiepileptic drugs (AED) [9–11], greater

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risk of suicidal behavior [12–14], increased complaints of cognitive deficit, and lower quality of life [15,16], as well as increased health-care costs [17]. While various anxiety syndromes may occur in association with epilepsy, GAD is characterized by disabling and persistent free-floating worry. In particular, GAD occurring in the context of epilepsy is often associated with fear of future seizures, fear of disease progression, or fear of specific complications [18,19].

Since psychiatric comorbidities are a worldwide problem in PWE [20], clinicians need diagnostic tools adapted for local language and culture. The ideal tool is a highly sensitive and highly specific self-questionnaire developed for rapid screening of these comorbidities in PWE [21]. These short and easily administered tools, which can readily be incorporated into routine clinical evaluation, i) help to counteract the tendency of underdiagnosis and suboptimal treatment of these psychiatric comorbidities, primarily in order to increase the quality of life of PWE, with the additional benefit of reducing health-care costs [20]; and ii) facilitate worldwide epidemiological investigation of the impact of psychiatric comorbidities in PWE once multiple language versions become available.

Concerning major depression in PWE, the Neurological Disorders Depression Inventory for Epilepsy (NDDI-E) has now been translated into over 10 languages and validated in native speaking populations, under the auspices of the International League Against Epilepsy (ILAE) Commission on Neuropsychiatry [22–32]. Increasing the worldwide availability of reliable screening tools for psychiatric comorbidities is indeed a priority goal of the ILAE Commission on Neuropsychiatry [33]. While screening for major depression has become easier with the NDDI-E, no such tool is currently widely available for screening for anxiety in epilepsy. As a consequence, GAD in epilepsy has not yet been extensively investigated [34] and clinicians still tend to underestimate its importance [22,35,36].

A self-reported symptom scale called the "GAD-7" was recently developed for primary care [37,38] and is a promising, reliable, and practicable tool for rapid screening of GAD in PWE [39,40]. This scale is similar to the NDDI-E as it is a self-reported questionnaire based on only a few items (7 for the GAD-7, and 6 for the NDDI-E), being shorter than classical self-reported screening questionnaires for GAD or MDE [41–44], which helps to optimize its use in a busy clinical practice. In addition, it seems particularly well suited as a potential screening tool in PWE since it contains no somatic items that might be confused with symptoms related to epilepsy or AED [36]. Given the differences in patient populations with different medical conditions and cultural and demographic factors (reflected in the variable cutoffs of questionnaires in different studies), validation of the GAD-7 specifically in PWE for each language is recommended [39]. The GAD-7 has been translated into multiple languages; the use of the GAD-7 in epilepsy has been so far validated in Korea and China [39,40] and used in Spain [45], and the need to validate this tool for PWE in other languages has been highlighted by the ILAE [21,33]. Thus, in the present study, we analyzed the psychometric properties of the French GAD-7 version in a representative sample of French PWE. In addition, we wished to assess whether different and complementary information was provided by the GAD-7 and the NDDI-E in our patient group.

2. Methods and materials

2.1. Participants

People with epilepsy were recruited from the Clinical Neurophysiology Department of the Marseille University Hospital and the Hôpital Henri Gastaut, Marseille (these 2 centers forming part of an integrated specialist tertiary epilepsy service) over an 11-month period (November 2014–September 2015). Included subjects were different from those in our previous study [32]. Inclusion criteria were: native French-speaking adult patients (>18 years of age) with any type of active epilepsy according to the ILAE criteria [46] and treated or not by AED. The diagnosis of epilepsy was documented clinically and confirmed where necessary with video-EEG investigations. Both inpatients and outpatients were included. Exclusion criteria were: insufficient capacity to consent and to understand and answer the self-report questionnaires and the presence of other severe chronic medical, neurological, and psychiatric conditions (other than epilepsy). Gender, age, type and frequency of seizures, age of onset of epilepsy, number of AED currently being taken, the presence of vagal nerve stimulation, and the use of antidepressant drugs were noted.

Patients were invited to participate in the study during their routine neurological evaluation. This study was conducted in accordance with the Declaration of Helsinki and French Good Clinical Practices. The study took place in a context of routine clinical care, since it consisted of using well-established patient questionnaires that are already in current clinical use, and whose use is indeed encouraged in epilepsy clinics as part of the evaluation. No intervention was involved. As such, specific Ethics Committe Approval for the study was not sought. On the other hand all patients were told of the study and gave their informed consent before taking part.

2.2. Procedure

2.2.1. Self-rated assessment

The GAD-7 [38,47], the Penn State Worry Questionnaire (PSWQ) [48,49], and the NDDI-E [22,32] were completed as part of the self-rated psychiatric assessment.

The GAD-7 consists of 7 items rated by the patients on a balanced four-point Likert scale ranging from "Not at all" (score = 0), "Several days" (score = 1), "More than half the days" (score = 2), to "Nearly every day" (score = 3) and takes less than 3 min to complete. The rating was determined according to patients' experience in the preceding two weeks. The French version of the GAD-7 was developed according to a forward–backward translation by 2 independent native French speakers and 2 independent native English speakers [38,47] and is freely downloadable on the patient Health Questionnaire website (www.phqscreeners.com). We assured the clarity and cultural acceptability of the French version of the GAD-7 in French PWE by administering it to 10 patients. This pretest showed no difficulties in understanding the items of the French GAD-7 in PWE. No adaptations were therefore required. The version of the French GAD-7 used in this study is shown in Table 1. The score ranges from 0 to 21. Used as screening tools for GAD, cutoffs were found with values of 6 to 9 [38–40].

The PSWQ consists of 16 items rated by the patients on a balanced five point Likert scale ranging from 1 ("not at all typical of me") to 5 ("very typical of me"). The PSWQ has previously been translated and validated in French [49]. The PSWQ is a score of severity of worry in the GAD [48]. The score ranges from 16 to 80. Used as screening tools for GAD, cutoffs were found with values of 45 to 65 [43,44,48].

The NDDI-E consists of 6 items rated by the patients on a balanced four-point Likert scale ranging from "never" (score = 1), "rarely" (score = 2), "sometimes" (score = 3), to "always or often" (score = 4) [22]. The rating was determined according to patients' experience in the preceding two weeks. The NDDI-E has previously been translated and validated in French PWE [32]. The score ranges from 6 to 24. An NDDI-E score that is higher than 15 indicates increased risk of a current episode of major depression in French PWE [32].

2.2.2. Psychiatric assessment

The generalized anxiety disorder module of the Mini-International Neuropsychiatric Interview (MINI) was completed as part of the psychiatric assessment before the self-rated assessment with the GAD-7, the PSWG, and the NDDI-E. This is a short structured questionnaire to identify GAD according to the criteria of the DSM-IV TR [50]. The MINI has previously been validated in French [51]. For the purposes of the present study, it was used as a gold standard for the diagnosis of current GAD.

2.3. Statistical analyses and hypotheses

Demographical and clinical data were compared between PWE with and without GAD using Chi^2 test for categorical variables and Student's t-test for continuous variables.