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Validation of diagnostic tests for depressive disorder in drug-resistant mesial temporal lobe epilepsy

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ABSTRACT

Purpose: This study aimed to evaluate the diagnostic accuracy of the Hamilton Rating Scale for Depression (HRSD), the Beck Depression Inventory (BDI), the Hospital Anxiety and Depression Scale (HADS), and the Hospital Anxiety and Depression Scale-Depression subscale (HADS-D) as diagnostic tests for depressive disorder in drug-resistant mesial temporal lobe epilepsy with hippocampal sclerosis (MTLE-HS).
Methods: One hundred three patients with drug-resistant MTLE-HS were enrolled. All patients underwent a neurological examination, interictal and ictal video-electroencephalogram (V-EEG) analyses, and magnetic resonance imaging (MRI). Psychiatric interviews were based on DSM-IV-TR criteria and ILAE Commission of Psychobiology classification as a gold standard; HRSD, BDI, HADS, and HADS-D were used as psychometric diagnostic tests, and receiver operating characteristic (ROC) curves were used to determine the optimal threshold scores.
Results: For all the scales, the areas under the curve (AUCs) were approximately 0.8, and they were able to identify depression in this sample. A threshold of ≥9 on the HRSD and a threshold of ≥8 on the HADS-D showed a sensitivity of 70% and specificity of 80%. A threshold of ≥19 on the BDI and HADS-D total showed a sensitivity of 55% and a specificity of approximately 90%. The instruments showed a negative predictive value of approximately 87% and a positive predictive value of approximately 65% for the BDI and HADS total and approximately 60% for the HRSD and HADS-D.
Conclusions: HRSD ≥ 9 and HADS-D ≥ 8 had the best balance between sensitivity (approximately 70%) and specificity (approximately 80%). However, with these thresholds, these diagnostic tests do not appear useful in identifying depressive disorder in this population with epilepsy, and their specificity (approximately 80%) and PPV (approximately 55%) were lower than those of the other scales. We believe that the BDI and HADS total are valid diagnostic tests for depressive disorder in patients with MTLE-HS, as both scales showed acceptable (though not high) specificity and PPV for this type of study.

1. Introduction

Epilepsy is a chronic disease associated with high rates of disability and functional impairment [1]. Mesial temporal lobe epilepsy (MTLE) is cited in a recent review [2] as an example of an aggressive epileptic condition that seems to have a relationship with increased seizure frequency and worsening cognitive function. In addition to disability and functional impairment, it is well known that there is a higher lifetime prevalence of mental disorders in people with epilepsy compared with the general population (23.5%) [3]; this prevalence reaches approximately 50% in patients with MTLE and drug-resistant epilepsy [4]. Depression is the most common psychiatric comorbidity found in patients with epilepsy [5]. It has been identified as a predictor of drug resistance [6], associated with a poorer result for epilepsy surgery [7,

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8] and related to unsatisfactory quality of life [9,10]. Despite the growing recognition of the importance of mood and anxiety disorders to the morbidity and mortality of patients with epilepsy, such disorders remain underrecognized and undertreated [11,12].

The diagnosis of depressive disorder is primarily based on the Diagnostic and Statistical Manual of Mental Disorders-Revised 4th edition (DSM-IV-TR) [13] for major depressive disorder (MDD) and the International League Against Epilepsy (ILAE) Commission of Psychobiology classification criteria [14] for interictal dysphoric disorder (IDD), a psychiatric comorbidity specifically associated with epilepsy. The application of these diagnostic standards usually requires psychiatric expert consultation, but this care is not always available, especially in countries with limited access to medical care. Diagnostic questionnaires can provide a viable alternative approach, depending on their accuracy and reliability.

Psychometric scales such as the Hospital Anxiety and Depression Scale (HADS) [15,16], the Hamilton Rating Scale for Depression (HRSD) [17–19], and the Beck Depression Inventory (BDI) [18,20,21] are widely used to screen for depression in clinical practice. Several studies investigating the available diagnostic tests for assessing depression comorbidity in epilepsy have shown that these tests have adequate performance and usefulness [22–24]. One study, however, found that sensitivity was low for most screening instruments, and the selection of instruments should consider the questions being addressed and the associated costs [25].

The purpose of the application of these scales in this patient population was to establish the presence of depressive disorder, which is known to be more prevalent than in the general population. Priority is given to highly specific tools that aimed to establish the presence of depressive disorder in a population of symptomatic but undiagnosed individuals. Because either sensitivity or specificity may be more relevant in different settings (i.e., clinical practice vs. research), it is possible to prioritize one over the other for a particular purpose. For example, the sensitivity would be more relevant in clinical practice, and the specificity would be more relevant in a research environment.

In the case of epilepsy, these scales have been used for diagnosing depression in heterogeneous samples composed of various types of epilepsy and epileptic syndromes. However, it is possible that the sensitivity and specificity of these diagnostic tests for depressive disorder when used in patients with epilepsy vary according to particular genetic and environmental characteristics and the severity of particular types of epilepsy and epileptic syndromes.

Mesial temporal lobe epilepsy is the most frequent form of drug-resistant epilepsy that is treated surgically [26]. It seems to be more closely associated with depressive disorders and with poorly controlled seizures compared to other types of epilepsy [27]. Moreover, seizure focus locations that involve the limbic structures (as in the case of temporal lobe epilepsy) are more strongly associated with depressive disorders compared with types of epilepsy that do not involve the limbic structures [28]. The neocortical and limbic structures involved in MTLE are also part of the neuronal network involved in depression; consequently, the sensitivity and specificity of diagnostic tests for depressive disorder could vary in MTLE compared to neocortical temporal lobe epilepsy, extratemporal epilepsies, or epilepsies related to thalamocortical synchronization mechanisms. Consistent with this idea, the results from one study involving healthy individuals suggest that hippocampal volume reduction may be associated with a predisposition toward developing depression [29]. The results from another study indicate that neuroimaging changes in patients with MTLE seem to be magnified when they are associated with comorbid, untreated depression, suggesting a neuroanatomical overlap between the two diseases [30].

For these reasons, this study aimed to validate diagnostic tests for detecting depressive disorder in a sample of Brazilian patients who are candidates for surgical treatment of drug-resistant mesial temporal lobe epilepsy with hippocampal sclerosis (MTLE-HS).

2. Methods

2.1. Subjects

One hundred three consecutive patients with drug-resistant MTLE-HS were enrolled. All patients underwent a presurgical evaluation at the Centro de Epilepsia de Santa Catarina (CEPESC) between October 2008 and March 2013, as well as a complete medical history, seizure semiology, neurological and neuropsychological examination, psychiatric interview, interictal and ictal video-EEG analyses, and magnetic resonance imaging (MRI) of their brain, as previously described [31,32]. Inclusion criteria were age older than 18 years, diagnosis of epilepsy according to the ILAE criteria [33], focal slowing, and interictal spikes and sharp waves over the anterior, inferior, and mesial temporal regions on an interictal scalp electroencephalogram (EEG). Furthermore, the patients were also required to have hippocampal atrophy on T1 and an increased hippocampal signal on T2 MRI sequences consistent with MTLE-HS [31,32]. Refractoriness was defined as a failure to respond to adequate trials of at least 2 antiepileptic drugs with a period of at least 12 months without seizures [34]. We excluded patients with extrahippocampal lesions, focal motor or sensory abnormalities on physical examination, generalized or extratemporal interictal spikes, and marked cognitive impairment that could confound the psychiatric and MTLE diagnosis. Patients presenting with acute psychotic symptoms during evaluation were also excluded from the study.

The sociodemographic features that were analyzed in the patients that met the inclusion criteria were sex, age, marital status, years of education, and occupation. The clinical data included epilepsy duration until the presurgical evaluation, monthly complex partial seizure frequency in the year before the psychiatric evaluation, the side of MTLE-HS, antiepileptic drug use (monotherapy or polytherapy) and current intake of antidepressants, defined as the use of antidepressants 30 days prior to the psychiatric interview.

The local Research Ethics Committee approved the study, and informed consent was obtained from all patients.

2.2. Psychiatric evaluation

The psychiatric interviews lasted approximately 120 min. During the interview, all patients were assessed alone first, and then with the caregiver, by a psychiatrist with experience in psychiatric comorbidities associated with epilepsy [7]. Axis I disorder diagnoses were classified according to a semistructured interview for the diagnostic algorithm of the DSM-IV-TR to determine the current presence of MDD. In this interview, the experienced psychiatrist actively sought to obtain data to complete the medical and psychiatric history of the patients and to perform the examination of their mental functions to investigate the diagnostic criteria established by the DSM-IV-TR. All patients were allocated to one of two groups: with or without depressive disorders. Moreover, we included in the former group the diagnosis of interictal dysphoric disorder (IDD), a psychiatric comorbidity specifically associated with epilepsy by the ILAE Commission of Psychobiology [14], in the depressive disorders group. Four psychiatric questionnaires were completed by each patient at the end of the interview. The patients completed the self-report scales (HADS, HADS-D, BDI), and finally, the same expert psychiatric interviewer administered the HRSD [15,19,21].

2.3. Diagnostic tests

The HADS was designed to measure psychological distress in nonpsychiatric inpatient populations [15]. It is widely used and consists of 14 multiple-choice items divided into anxiety and depression subscales. The items are rated on a 4-point Likert scale scored from 0 to 3, resulting in a final score ranging from 0 to 21. Bjelland et al. [35] found that a cutoff score of 8 + on the HADS-D had a sensitivity and specificity of approximately 0.80 in a general nonpsychiatric population, with a better