Rapid detection of major depression in epilepsy: a multicentre study

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Summary

Background Depression is a common comorbid disorder in epilepsy but is not routinely assessed in neurology clinics. We aimed to create a rapid yet accurate screening instrument for major depression in people with epilepsy.

Methods We developed a set of 46 items to identify symptoms of depression that do not overlap with common comorbid cognitive deficits or adverse effects of antiepileptic drugs. This preliminary instrument and several reliable and valid instruments for diagnosis of depression on the basis of criteria from the Diagnostic and Statistical Manual IV, depression symptom severity, health status, and toxic effects of medication were applied to 205 adult outpatients with epilepsy. We used discriminant function analysis to identify the most efficient set of items for classification of major depression, which we termed the neurological disorders depression inventory for epilepsy (NDDI-E). Baseline data for 229 demographically similar patients enrolled in two other clinical studies were used for verification of the original observations.

Findings The discriminant function model for the NDDI-E included six items. Internal consistency reliability of the NDDI-E was 0·85 and test-retest reliability was 0·78. An NDDI-E score of more than 15 had a specificity of 90%, sensitivity of 81%, and positive predictive value of 0·62 for a diagnosis of major depression. Logistic regression showed that the model of association of major depression and the NDDI-E was not affected by adverse effects of antiepileptic medication, whereas models for depression and generic screening instruments were. The severity of depression symptoms and toxic effects of drugs independently correlated with subjective health status, explaining 72% of variance. Results from a separate verification sample also showed optimum sensitivity, specificity, and predictive power at a cut score of more than 15.

Interpretation Major depression in people with epilepsy can be identified by a brief set of symptoms that can be differentiated from common adverse effects of antiepileptic drugs. The NDDI-E could enable rapid detection and improve management of depression in epilepsy in accordance with internationally recognised guidelines.

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Introduction

The diagnosis of major depression in non-psychiatric clinical settings has received much attention in recent years.[1,2] WHO and other national and international health advocacy agencies have explicit guidelines for diagnosis and treatment of major depression in primary care.[3–5] In view of the available evidence, which indicates that major depression is not routinely assessed in neurology clinics,[6] and the fact that most affected patients are subsequently not treated,[7] substantial opportunity exists to improve the quality of care for many people with epilepsy.

Depression is a common comorbid disorder in epilepsy. The prevalence of depressive disorders is reported to be more than 30% in community-based epilepsy samples[8] and 20–55% in specialist epilepsy clinics.[9–11] These rates seem to be higher than in other chronic non-neurological illnesses,[12] and could be associated with specific underlying brain dysfunction.[6,13–16] Depression is a strong predictor of self-perceived health status, independent of seizure rate,[7,17–20] and is associated with increased health-care costs of epilepsy.[21] Furthermore, suicidal ideation and suicide are significantly increased in patients with epilepsy compared with the general population.[22] The relatively high prevalence and subsequent increased disability and mortality make the identification and treatment of major depression important for the optimum management of individuals with epilepsy.[23,24]

Various factors associated with epilepsy could adversely affect the accuracy of a screening technique for depression. For example, side-effects of antiepileptic drugs, such as decreased concentration, fatigue, and sleep disturbance, could overlap with somatic symptoms of depression, as could memory problems, which commonly occur in temporal lobe epilepsy. Also, patterns of symptoms can be atypical in some mood disorders common to epilepsy.[25–27] These confounders could alter the sensitivity and specificity of a screening tool.

The lack of a brief and uncomplicated screening technique specifically designed for use in the outpatient neurology clinic setting could contribute to existing limitations in management. We therefore undertook a multicentre study to assess major depression in epilepsy to develop a brief yet accurate screening technique.

Methods

Participants

Individuals were recruited from outpatient epilepsy clinics of five participating academic medical centres (Stanford University, University of Wisconsin-Madison, Rush University, Georgetown University, and Washington

	Non-depressed (n=170)	Major depression (n=35)
Mean age, years (SD)	38·8 (11·9)	41·5 (11·7)
Sex		
Male	60 (35%)	10 (29%)
Female	110 (65%)	25 (71%)
Ethnic group		
White	130 (76%)	28 (80%)
Black	28 (16%)	3 (9%)
Asian	3 (2%)	0
American Hispanic	7 (4%)	3 (9%)
Other	2 (1%)	1 (3%)
Marital status*		
Married	72 (42%)	12 (34%)
Divorced	21 (12%)	9 (26%)
Widowed	5 (3%)	3 (9%)
Single	72 (42%)	9 (26%)
Employment status		
Retired	4 (2%)	2 (6%)
Employed full-time	66 (39%)	10 (29%)
Employed part-time	16 (9%)	3 (9%)
Full-time student	12 (7%)	2 (6%)
Unemployed	43 (25%)	12 (34%)
Homemaker	13 (8%)	3 (9%)
Other	16 (9%)	3 (9%)
Mean WRAT score (SD)	96·4 (13·5)	96·9 (13·7)
Seizure type		
Simple partial	49 (29%)	14 (40%)
Complex partial	98 (58%)	20 (57%)
Partial evolving to secondary general	59 (35%)	13 (37%)
Absence	16 (9%)	4 (11%)
Myoclonic	8 (5%)	1 (3%)
Clonic	2 (1%)	0
Tonic	2 (1%)	1 (3%)
Tonic-clonic	57 (34%)	9 (26%)
Atonic	2 (1%)	0
Mean time since onset of non-febrile seizures, years (SD)	18·3 (12·9)	18·6 (13·1)
Currently taking medication for depression†	30 (18%)	17 (49%)

Data are number (%) unless otherwise stated. WRAT=wide range achievement test-3. *Two people in the depressed group did not disclose their marital status. †χ^2=18·4, p<0·001; no other significant between group differences.

Table 1: **Demographic and clinical characteristics of the study sample**

	Always or often	Sometimes	Rarely	Never
Everything is a struggle	4	3	2	1
Nothing I do is right	4	3	2	1
Feel guilty	4	3	2	1
I'd be better off dead	4	3	2	1
Frustrated	4	3	2	1
Difficulty finding pleasure	4	3	2	1

For the statements in the table, patients are asked to circle the number that best describes them over the past 2 weeks including the day of the assessment.

Table 2: **Items determined by the discriminant function analysis as the optimum model for identification of major depression (presented as the NDDI-E)**

University). The study protocol and informed consent documents were approved by the human subjects protection committees at each institution. Patients provided written informed consent before study enrolment. Inclusion criteria were: age 18 years or older; current diagnosis of epilepsy requiring treatment with one or more antiepileptic drugs; stable dose of the antiepileptic drug regimen for at least the past 30 days; a score of more than 69 on the wide range achievement test-3 (WRAT-3) to ensure adequate reading ability to complete self-report forms; and ability to provide informed consent and comply with the study protocol. Exclusion criteria were: current treatment with vagal nerve stimulation; presence of clinically significant medical or psychiatric comorbidity (eg, psychosis or delirium) that could, in the opinion of the investigator, prevent accurate completion of the study questionnaires; and inability to speak or read English adequately to follow the study protocol. A separate cohort of patients from two clinical studies (one with similar inclusion and exclusion criteria) was used for validation of the observations from the original sample. One of these studies included two sites (Columbia University and Washington University) that contributed 70 participants and the other was a 15-site study that enrolled 159 patients.

Procedures

The multidisciplinary research team composed of two neurologists (KJM, FGG), a psychiatrist (JJB), a neuropsychologist (BPH), and a physician who was board certified in both neurology and psychiatry (AMK). All had substantial experience of clinical research in epilepsy and associated neuropsychological problems. Each of the investigators was asked to provide items or phrases that would identify symptoms of depression that would not be similar to common adverse effects of antiepileptic drugs—eg, decreased concentration or appetite change—or cognitive problems commonly reported in people with epilepsy—eg, memory dysfunction. The initial instrument consisted of a total of 46 unique items, with each item scored on a Likert-like scale. A stepwise method for the discriminant analysis (SPSS version 11.0.1) was used to ascertain the most efficient set of items that correctly classified patients as having major depression or not based on the mini international neuropsychiatric interview (MINI).[28] The MINI is a previously validated interviewer-administered, structured, diagnostic, psychiatric interview that renders a dichotomous classification of major psychiatric disorders. To assess consistency and validity of the discriminant analysis we compared the Wilk's lambda and unexplained variance methods as well as F value (entry 3·84; removal 2·71) and probability of F (entry 0·05; removal 0·1) criteria.

Statistical analysis

For the items selected for the neurological disorders depression inventory for epilepsy (NDDI-E) by the