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BRIEF COMMUNICATION

Do mood instability symptoms in epilepsy represent formal bipolar disorder?

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Summary

We aimed to assess rates of bipolar symptoms versus bipolar disorder in epilepsy, and the effect of bipolar symptoms on quality of life (QOL) in epilepsy. Bipolar, disability, and QOL instruments were administered to 99 tertiary epilepsy center patients. Patients who scored positive on the Mood Disorder Questionnaire (MDQ) also completed depression scales and a structured psychiatric interview. Results indicated MDQ+ patients (10.1%) had worse QOL and more work, social, and family life disruptions. Most MDQ+ patients did not have bipolar disorder. There was close overlap between depressive and bipolar symptomatology. Based on results of this study, bipolar symptom is not synonymous with bipolar *disorder*. Symptoms picked up by the MDQ may be epilepsy-related depressive symptoms. Bipolar symptoms are associated with more disability, worse QOL, and may have treatment implications.

KEY WORDS: Epilepsy, Bipolar, Depression.

Bipolar disorder is a psychiatric condition characterized by cyclical changes in mood and behavior.

A previous community-based study performed by our group using the Mood Disorder Questionnaire (MDQ), a validated self-report screening instrument for the presence of a lifetime history of bipolar disorder (Hirschfeld et al., 2003), demonstrated that 12.2% of patients with epilepsy had bipolar symptoms, representing higher rates than those found in other chronic conditions or a healthy comparison group (Ettinger et al., 2005). However, the MDQ has not been validated in the epilepsy population. In addition, the interictal dysphoric disorder (IDD) has also been shown to manifest symptoms of mood instability in neurologic disorders such as epilepsy (Blumer, 2000) and migraine. A recent study further demonstrated that bipolar symptoms frequently observed in patients with epilepsy are most likely related to phenotype copies of bipolar disorder, such as IDD of epilepsy, postictal manic or hypomanic states, and preictal dysphoria (Mula et al., 2008).

In this study, we aimed to assess the rate of bipolar symptoms as measured by the MDQ in tertiary epilepsy center patients and the effect of a positive MDQ score on quality of life (QOL), and to clarify whether a positive MDQ score indicates an actual diagnosis of bipolar disorder.

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Methods

This study was approved by the North Shore-LIJ Health System Institutional Review Board prior to study initiation. All enrolled patients provided written informed consent.

Patient population

Adult epilepsy patients aged 18 or older capable of completing self-reporting questionnaires were consecutively recruited at the Comprehensive Epilepsy Center at the LIJ Medical Center. Diagnosis of epilepsy was rendered by center epileptologists based upon assimilation of clinical and electroencephalographic data. Patients with mental retardation or psychogenic nonepileptic seizures (PNES) were excluded.

Study design

This involved an initial screening and subsequent additional testing phase. There were two office visits and there was one telephone interview. At visit 1, all patients completed a battery of self-reporting questionnaires: (1) MDQ, a bipolar disorder screening tool validated in psychiatric outpatients (specificity = 0.90, sensitivity = 0.73) and the general U.S. population (specificity = 0.97, sensitivity = 0.28), with an optimal cutoff of ≥7 items (Hirschfeld et al., 2003); (2) Bipolar Spectrum Diagnostic Scale (BSDS), another validated instrument for bipolar disorder

screening (specificity = 0.93, sensitivity = 0.75) based on an optimum threshold score of ≥13 (Ghaemi et al., 2005); (3) the three-item Sheehan Disability Scale (SDS), measuring mental health-related functional impairments (Sheehan, 1983); and (4) the Quality of Life in Epilepsy-89 (QOLIE-89) inventory, a validated 89-question instrument measuring health-related QOL in epilepsy (Devinsky et al., 1995).

MDQ-positive (MDQ+) patients returned for visit 2 to complete the following testing. (1) the Center for Epidemiologic Studies Depression Scale (CES-D), a 20-item depression symptom scale (Radloff, 1977). CES-D scores of 0–14 signify no depression, 15–21 mild depression, and ≥22 major depression (Katz et al., 2006). (2) The Neurological Disorders Depression Inventory for Epilepsy (NDDI-E), a six-item questionnaire validated to screen for major depression in epilepsy (specificity = 0.90, sensitivity = 0.81) with a cutoff score >15 (Gilliam et al., 2006). (3) A psychiatric interview consisting of the Structured Clinical Interview For DSM-IV (SCID) Modules A & D and Mini International Neuropsychiatric Interview (MINI), Version 5.0.0, Section L (Psychotic disorder; Sheehan et al., 1998).

Statistical analysis

Comparisons between MDQ positive screens (n = 10) and negative screens (n = 89) on demographic variables (gender, race, ethnicity, and age) were conducted using chi-square tests for pair-wise comparisons. A two by two cross-stab looked at MDQ scale results (positive vs. negative cases) and BPSD scale results (positive vs. negative cases) and tested this relationship using Fisher's exact test. Differences in QOLIE subscale means and overall QOLIE scale means were tested across MDQ+ and MDQ− groups using *t*-tests for independent samples.

Results

We enrolled 101 patients; data from 2 patients were excluded due to their subsequent diagnosis of PNES after enrollment. Of 99 patients, 10 (10.1%) had a positive MDQ screening for bipolar symptoms. There were no statistically significant differences in demographic profiles (gender, race, ethnicity, and age) between the MDQ+ and MDQ− groups.

BSDS was consistent with the MDQ, finding a statistically significant difference in the prevalence of bipolar symptoms between the MDQ+ and MDQ− groups ($p < 0.001$) (Fig. 1). The MDQ+ group scored higher on all three SDS disruption categories (means ± standard deviation): work (6.14 ± 2.34 vs. 2.91 ± 3.17, $p = 0.012$), social life (6.20 ± 3.22 vs. 3.07 ± 3.11, $p = 0.003$), and family life/home responsibilities (7.40 ± 2.88 vs. 3.35 ± 3.45, $p = 0.001$).

The MDQ+ group had statistically significant lower QOLIE-89 overall T-score than the MDQ− group (40.00 ± 7.53 vs. 48.99 ± 10.17, $p = 0.01$), and it also scored significantly lower ($p < 0.05$) in 6 of the 17 QOLIE-89 primary scales: Role limitations—emotional, work/driving/social function, emotional well-being, seizure worry, medication effects, and social isolation. The T-score differentials for the remaining scales, although not statistically significant, did trend in the expected direction.

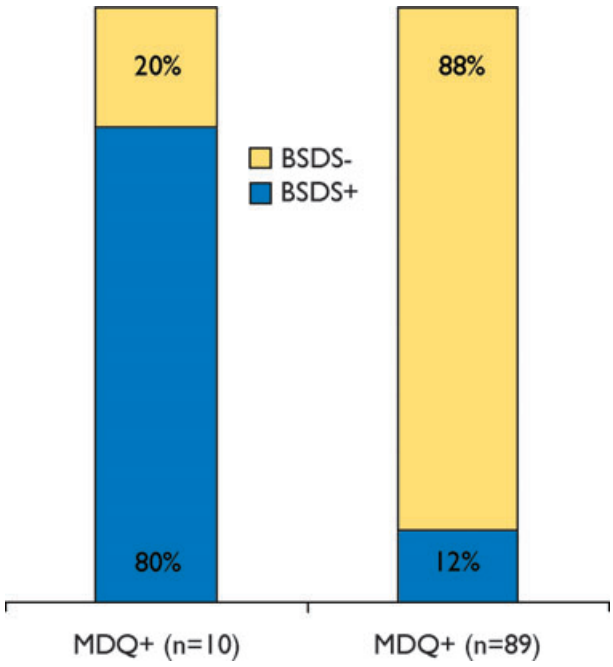

Figure 1.
A breakdown of the percentage of patients screening positive (BSDS+) or negative (BSDS−) for bipolar symptoms in the BSDS among the MDQ+ and MDQ− groups.
Epilepsia © ILAE

Of the 10 MDQ+ patients, 7 returned for visit 2 and 3 were lost to follow-up. Demographic information, psychiatric interview outcomes, and questionnaire results of these patients are summarized in Table 1.

Discussion

In our tertiary epilepsy center population, 10.1% met criteria for bipolar symptomatology on the MDQ, which is similar to our finding in a community-based study (12.2%) (Ettinger et al., 2005). These findings suggest that it would be valuable to screen for bipolar symptoms in patients with epilepsy. Such patients may warrant further psychiatric evaluation and treatment. Finding bipolar symptoms may have implications in the selection of antiepileptic drugs (AEDs), which may have distinct positive or negative psychotropic effects. Future studies with larger samples should examine the potential association between specific AEDs administered and patients' mood symptoms.

Demographic factors did not predict who had bipolar symptoms, suggesting that other factors may play a role.

Table 1. Demographic and scale scores for MDQ-positive respondents

Sex	Age	Race	SCID diagnosis	BSDS+[a]	Overall QOLIE-89[b]	CES-D+[c]	NDDI-E+[d]
F	24	White	No mood disorder	Yes	49	Mild	Yes
F	43	White	ND	Yes	42	ND	ND
F	60	White	PTSD, Dysthymia	Yes	43	Mild	No
F	44	Black	No mood disorder	Yes	39	Mild	Yes
M	47	White	Depressive disorder NOS (Past)	Yes	47	Major	No
F	48	Black	Simple bereavement (Past)	No	44	Major	No
F	49	Other	Current severe Dysthymia, past major depression	Yes	26	Major	Yes
F	54	White	Bipolar disorder II (current rapid cycling without full inter-episode recovery)	Yes	45	Major	Yes
M	19	White	ND	No	31	ND	ND
F	49	White	ND	Yes	36	ND	ND

ND, not done.
[a]Bipolar Spectrum Diagnosis Scale (BSDS) Positive (score ≥13).
[b]QOLIE-89 transformed T-score with mean of 50 and standard deviation (SD) of 10.
[c]Center for Epidemiologic Studies Depression Scale, positive score (0–14, no depression; 15–21, mild depression; ≥22, major depression).
[d]NDDI-E, positive score (>15).

Future studies should delve further into potential biological, epilepsy-related, and psychosocial risk factors for bipolar symptoms.

The results from MDQ and BSDS were similar, but more patients with epilepsy screened positive for BSDS than for MDQ. One explanation may be BSDS is highly sensitive and specific for bipolar spectrum illness, whereas MDQ is less effective in detecting milder manic symptoms (Ghaemi et al., 2005).

Patients with MDQ bipolar symptomatology experienced functional impairment in work, social life, and family/home life, as well as QOL impairments. These findings lend further importance to the value of screening for bipolar symptomatology, as such patients may need psychosocial intervention. Alternatively, it is possible that the MDQ is really detecting epilepsy-associated depression, which has been well-demonstrated in prior studies to correlate well with adverse quality of life.

There was overlap between depressive symptomatology and bipolar symptomatology, especially CES-D. Only one of the seven interviewed MDQ+ patients had formal bipolar disorder, but all of them met criteria for some depressive symptomatology. Therefore, MDQ may be in some cases picking up mood instability common in depression of epilepsy. Our results are in agreement with a recent study that demonstrated that 43% of epilepsy patients with positive MDQ screening were diagnosed with IDD, and that only 14% had ''pure'' bipolar symptoms (Mula et al., 2008). Mood instability symptom severity as measured by the MDQ may not meet criteria of DSM-IV–based bipolar disorder diagnosis.

Our study is limited by the small sample size, especially those with positive MDQ screening. Further studies should attempt to delineate roles of specific epilepsy-related factors such as epilepsy type, seizure medications, psychiatric factors, family history, and psychosocial variables. In addition, our reported results lay the foundation for a more ambitious study to formally assess validity and reliability of the MDQ in patients with epilepsy.

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Disclosure

The remaining authors have no conflicts of interest. We confirm that we have read the Journal's position on issues involved in ethical publication and affirm that this report is consistent with those guidelines.

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