Epilepsy in Bipolar Disorder: Impact on Clinical Features, Course and Outcome

Sarah Knott[1], Michael Kerr[2], Katherine Gordon-Smith[1], Lisa Jones[1], Nick Craddock[2], Ian Jones[2], Liz Forty[2]

[1]Division of Psychological Medicine and Clinical Neurosciences, Cardiff University, UK
[2]Department of Psychological Medicine, University of Worcester, UK

Introduction

Several converging lines of research suggest a relationship between bipolar disorder (BD) and epilepsy. Both conditions: are substantially heritable; follow an episodic course; can be chronic; and respond to anticonvulsant medications, all of which suggest a common underlying pathophysiology [1]. It is well recognized that mood disorders and epilepsy commonly co-occur. The psychiatric comorbidity of epilepsy has been well described, with mood disorders reported to occur at much greater rates than the background prevalence (between 20-50%) [2]. However, to date, much of the neuropsychiatric literature has focused on the study of unipolar depression with investigation into BD remaining limited. In addition, there has been a distinct lack of studies exploring the assessment of epilepsy within a bipolar population. The present study looked to explore the comorbid relationship between BD and epilepsy. A primary aim of the study was to assess the rate of self-reported epilepsy within a large, well-characterised sample of UK participants with a DSM-IV [3] diagnosis of BD. The secondary aim was to explore the relationship between self-reported epilepsy and the clinical features and course of the bipolar illness.

Methods

Sample: This study utilised rich clinical data collected through the Bipolar Disorder Research Network (BDRN); a large, well-defined sample of UK participants (N>6000) with a DSM-IV diagnosis of bipolar disorder (bipolar I disorder, bipolar II disorder, or schizoaffective bipolar type).

Assessment: BDRN participants were screened for a lifetime history of epilepsy/seizure disorder via a self-report questionnaire; a modified version of a brief screening instrument to identify individuals with epilepsy, designed by Ottman et al (2010) [4]. 1596 individuals completed the questionnaire and so were included in the study.

Data analysis: Demographic and lifetime bipolar clinical characteristics were compared between bipolar subjects with and without a self-reported history of epilepsy. Comparisons were made using Mann Whitney-U tests for continuous variables 2x2 chi square tests for categorical variables. Variables significant within univariate analyses were entered into a logistic regression model to identify variables that best predicted the presence of epilepsy.

Results

Table 1. Demographic and bipolar illness variables according to the presence of comorbid epilepsy

	BD+epilepsy (n=127)	BD-epilepsy (n=1386)	P-value
Age at interview Median (IQR) Range	47.50 (15) 22-69	49 (17) 20-84	.632
Female, n (%)	86 (68.3%)	974 (70.3%)	.635
Ever married, n (%)	112 (89.6%)	1146 (85.4%)	.198
Post-secondary education, n (%)	78 (67.8)	969 (74.6%)	.112
Systematic recruitment, n (%)	35 (28.1%)	360 (26.8%)	.770
Family history of affective disorders, n (%)	92 (83.6%)	991 (86.2%)	.464
DSM-IV diagnosis BPI BPII SABP	85 (67.7%) 36 (28.3%) 5 (3.9%)	940 (67.8%) 400 (28.9%) 46 (3.3%)	.928
Age of BD onset Median (IQR) Range	20 (15) 9-51	21 (12) 5-64	.528
No. episodes mania Median (IQR) Range	5.1 (7.1) 1-100.1	5.1 (8) 1-300	.884
No. episodes depression Median (IQR) Range	10 (15.1) 0-100.1	8 (16) 0-150.1	.068
Psychotic features, n (%)	60 (64.4%)	733 (61.1%)	.471
Rapid cycling, n (%)	30 (23.8%)	291 (21.1%)	.475
Suicide attempt, n (%)	79 (64.2%)	631 (47.4%)	**.0003**
History of psychiatric section, n (%)	41 (33.9%)	498 (37.6%)	.417
GAS Mania Median (IQR) Range	39.50 (30) 10-60	35 (30) 5-65	.652
GAS Depression Median (IQR) Range	40 (14) 3-80	40 (15) 10-81	.155
BADDS Mania Median (IQR) Range	83 (5.03) 40-99	83 (5) 20-100	.500
BADDS Depression Median (IQR) Range	76 (22.6) 0-99	69.5 (22) 0-100	.194
BADDS Psychosis Median (IQR) Range	21 (18.25) 10-99	22 (19) 1-100	.876

Table 2. Psychiatric comorbidity within bipolar disorder according to the presence of comorbid epilepsy

	BD+epilepsy (n=127)	BD-epilepsy (n=1386)	P-value
Depression, n (%)	84 (84%)	983 (88.2%)	.213
Schizophrenia, n (%)	3 (3.1%)	77 (6.9%)	.154
Agoraphobia, n (%)	10 (10.1%)	51 (4.6%)	**.017**
Panic disorder, n (%)	29 (29.6%)	175 (16.1%)	**.001**
Phobias, n (%)	13 (13.6%)	63 (5.7%)	**.004**
Generalised anxiety disorder, n (%)	67 (67.7%)	648 (59.1%)	.096
Alcohol abuse, n (%)	18 (18.6%)	119 (10.6%)	**.017**
Other substance abuse, n (%)	10 (10.2%)	45 (4%)	**.009**

A comparison of demographic characteristics, bipolar illness variables, and psychiatric comorbidity between bipolar subjects with and without a history of epilepsy is presented in **tables 1** and **2**.

Variables significant at the $p < .05$ level were included as explanatory variables in a logistic regression model with absence or presence of epilepsy as the dependent variable. Multivariate analysis revealed a significant association between self-reported epilepsy and a history of suicide attempt (OR: 1.790, 95% CI: 1.130-2.836, p=.013, Wald: 6.162, df=1). Within-group analysis revealed that this association did not appear to be explained by medication effects, with rates of lithium and antidepressant medication being similar between epilepsy and no epilepsy groups. (**figures 1** and **2**).

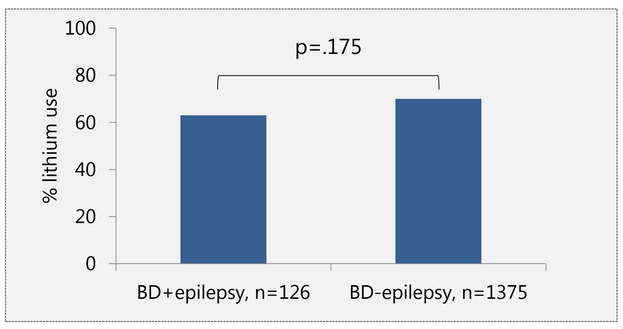

Figure 1. Rate of lithium use across bipolar subjects with and without comorbid epilepsy

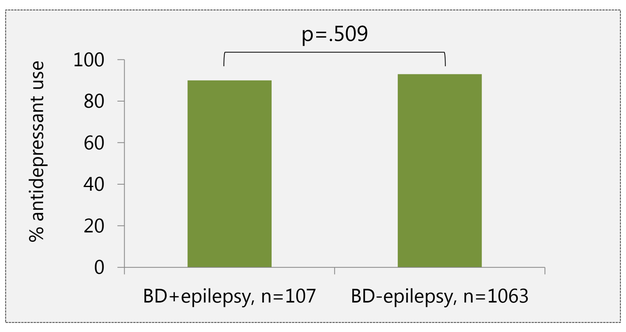

Figure 2. Rate of anti-depressant use across bipolar subjects with and without comorbid epilepsy

In 2008, the Food and Drug Administration (FDA) issued a controversial alert regarding a two-fold increased risk of suicidal thoughts and behaviour related to the use of anti-epileptic drugs (AEDs). [5] Therefore, it is possible that the increased risk of suicide attempt observed in bipolar subjects with comorbid epilepsy may be related to the increased use of anti-epileptic medication.

An increased rate of AED use was observed within bipolar subjects with comorbid epilepsy who had a history of suicide attempt compared to those without such history, however this was not found to be statistically significant (46.3% vs. 34.2%, p=.229).

Conclusions

Results demonstrate an increased rate of epilepsy in the BD sample, compared to that reported in the general population (Ottman et al., 2010). Multivariate analysis revealed an independent association of a history of suicide attempt with self-reported epilepsy within individuals with BD, and this relationship did not appear to be explained by medication effects. Exploratory analysis (not presented here) revealed that the association between epilepsy and suicide attempt within BD persisted even after adjusting for significantly associated bipolar and epilepsy-related illness variables, as well as co-existing psychiatric and chronic medical conditions.

The current study highlights the importance of recognising and identifying comorbid epilepsy within individuals with BD, particularly given the association of epilepsy with important illness outcomes, including increased suicidality. In addition, comorbid epilepsy within BD may provide an attractive opportunity for subcategorising for future genetic studies, potentially facilitating the identification of shared pathophysiological mechanisms.

Limitations: Self-reported definition of epilepsy. Due to the modest number of bipolar subjects with comorbid epilepsy and limited statistical power, corrections were not routinely made for multiple testing.

References

[1]**Knott, S et al. (2015).** Epilepsy & bipolar disorder. Epilepsy Behav, 52: 267-74.
[2]**Kanner, AM. (2003).** Depression in epilepsy: prevalence, clinical semiology, pathogenic mechanisms and treatment. Biol Psychiatry, 54: 388–398.
[3]**American Psychiatric Association. (2000).** Diagnostic and statistical manual of mental disorders: DSM- IV (4th ed). Washington, DC: American Psychiatric Association
[4]**Ottman, R et al. (2010).** Validation of a brief screening instrument for the ascertainment of epilepsy. Epilepsia, 51(2):191–197.
[5]**Food and Drug Administration. (2008).** Statistical Review and Evaluation: Antiepileptic Drugs and Suicidality. US Department of Health and Human Services, FDA Centre for Drug Evaluation and Research, Office of Translational Sciences, Office of Biostatistics 2008.

Acknowledgements

I would like to thank all of the members of BDRN and participants who have very kindly taken part for making this research possible.

Supported by wellcome trust

THE STANLEY MEDICAL RESEARCH INSTITUTE

www.bdrn.org
moodresearch@worc.ac.uk
s.knott@worc.ac.uk