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Research report

More pernicious course of bipolar disorder in the United States than in many European countries: Implications for policy and treatment

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ABSTRACT

Background: There is some controversy but growing evidence that childhood onset bipolar disorder may be more prevalent and run a more difficult course in the United States than some European countries.
Methods: We update and synthesize course of illness data from more than 960 outpatients with bipolar disorder (average age 40) from 4 sites in the U.S. and 3 sites in Netherlands and Germany. After giving informed consent, patients reported on parental history, childhood and lifetime stressors, comorbidities, and illness characteristics.
Results: Almost all aspects of bipolar disorder were more adverse in patients from the US compared with Europe, including a significantly higher prevalence of: bipolar disorder in one parent and a mood disorder in both parents; childhood verbal, physical, or sexual abuse; stressors in the year prior to illness onset and the last episode; childhood onsets of bipolar illness; delay to first treatment; anxiety disorder, substance abuse, and medical comorbidity; mood episodes and rapid cycling; and nonresponse to prospective naturalistic treatment.
Limitations: Selection bias in the recruit of patients cannot be ruled out, but convergent data in the literature suggest that this does not account for the findings. Potential mechanisms for the early onset and more adverse course in the U.S. have not been adequately delineated and require further investigation.
Conclusions: The data suggest the need for earlier and more effective long-term treatment intervention in an attempt to ameliorate this adverse course and its associated heavy burden of psychiatric and medical morbidity.

1. Introduction

Recent epidemiological data indicate a 3% to 5% lifetime prevalence of bipolar disorder in the United States and many other countries throughout the world (Merikangas et al., 2010). Yet there is considerable ongoing controversy about the diagnosis of bipolar disorder in childhood and adolescence and its apparent increase in the United States compared to some European and Asiatic countries. This controversy has to some extent diverted efforts from early recognition, diagnosis, and treatment, and has contributed to the relative paucity of treatment related research in childhood onset bipolar disorder (Post, 2009).

Data from naturalistic follow-up studies of childhood onset bipolar illness in the US indicate that patients are ill some two

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thirds of the time of follow-up, and while most show periods of remission, relapses are common (Birmaher et al., 2009a, 2009b; DelBello et al., 2007; Geller et al., 2008, 2010; Wozniak et al., 2011). These data mirror those from studies in adults which suggest that patients are ill approximately 50% of the time of long-term follow-up with 3 times more time depressed than time manic (Judd et al., 2002; Kupka et al., 2007).

Given these evolving views of the nature of bipolar disorder, its morbidity, and its high degree of treatment resistance in both children and adults, we wished to examine comparative characteristics in patients emanating from the United States compared to some European countries. In our bipolar collaborative network (originally called Stanley Foundation Bipolar Treatment Outcome Network) we had the opportunity to compare adult outpatients from 4 sites in the United States compared to 3 in Europe. While some of the initial findings in a subset of subjects comparing bipolar illness on the two continents have been published (Post et al., 2010a, 2011, in press-a), we thought a more up to date and comprehensive presentation and overview of the findings in the context of the existing literature would be clinically and heuristically valuable.

2. Methods

979 patients with bipolar disorder were enrolled into the Stanley foundation bipolar treatment outcome network from 1995 to 2002 (Kupka et al., 2007; Post et al., 2001, 2010a, 2011, in press-a,b). They gave informed consent for their participation and completed a comprehensive battery of diagnostic and follow-up evaluations. This included a SCID interview to confirm the diagnosis and cross-sectional ratings on the young mania rating scale (YMRS) and the inventory for depressive symptoms (IDS), as well as the clinical global impression scale for bipolar disorder (CGI-BP) at each visit. In addition patients were rated on a daily basis on the NIMH-life chart method (NIMH-LCM) by trained clinicians.

Upon enrollment, patients completed a detailed questionnaire that included data on: demographics; clinical course of illness; parental history of psychiatric disorder; and psychosocial stress in childhood, at illness onset, and prior to the last episode. It also included information about comorbid anxiety, substance abuse, and medical conditions. Age of illness onset was acquired from both a SCID interview and the patient questionnaire in response to the inquiry about the age of onset of first hypomanic or manic episode or the first episode of depression associated with dysfunction.

Upon network entry, the subset of 529 patients who were in the network for at least 1 year were classified as well (relatively euthymic) if they were minimally impacted by manic and depressive symptoms and maintained this state for another 6 months of prospective treatment in the network. In those who entered the network ill, based on the daily NIMH-LCM, patients were characterized as long-term (greater than 6 months) responders or non-responders based on their ability to achieve and maintain a much improved or very much improved clinical status on the CGI BP.

In each area of genetic and environmental vulnerability, course of illness characteristics, and retrospective and prospective treatment responsiveness, patients emanating from the 4 sites in the US (Los Angeles, Dallas, Cincinnati, Bethesda) were compared with those from the 3 sites and Europe (Utrecht, Freiberg, Munich). Some data were previously published on the subset of 529 patients who had been rated prospectively and had continuous data for at 1 year (Post et al., 2010a, 2010b, 2011; in press-b). Here we update the data on the entire cohort of 979 patients who entered the network and completed the questionnaire and rating forms. This included patients from the US sites ranging from an N of 653 to 687 and a range of 287 to 292 from European sites depending on the variable examined (Table 1).

3. Results

3.1. More genetic and environmental vulnerability (in the US than in Europe)

Since the family history data was based on the opinion of the proband and not on interviews with each family member, we chose to examine only parental diagnosis for unipolar and bipolar

Table 1

Demographic and clinical characteristics of US and European populations

	n	Overall	US	Europe	χ	*p*	
Overall population		968	676	292			
Gender (% female)	967	56.7%	57.9%	53.8%	1.4	0.231	
Age onset (less than 19)	938	41.5%	69.2%	34.3%	99.8	0.00	
Race (% white)	961	91.5%	89.5%	95.9%	10.5	0.001	
	n	Overall	US	Europe	*t*/*z*	*p*	
Mean age at entry (yrs)	967	40.5	40.6	40.3	0.38 (*t*)	0.07	
Mean age of onset (years)	940	19.4	17.2	24.2	−9.95 (*z*)	0.00	
Mean age of onset depression (years)	915	20.1	18.1	24.8	−10.34 (*z*)	0.00	
Mean age of onset mania (years)	916	23.4	21.3	27.9	−9.87 (*z*)	0.00	
	n	0	1–4	5–20	20+	χ	*p*
Depressive episodes (US)	648	2.6%	15.3%	24.1%	58.0%	102.7	0.00
Depressive episodes (Europe)	282	4.6%	36.7%	35.1%	23.4%		
Manic episodes (US)	650	2.3%	21.1%	31.2%	45.4%	75.8	0.00
Manic episodes (Europe)	295	2.5%	43.9%	35.1%	18.6%		
	n	0	1	2–4	5+	χ	*p*
Depressive hospitalizations (US)	652	4 48.3%	2121.9%	18.4%	11 11.4%	1 14.5	0.002
Depressive hospitalizations (Europe)	283	35.0%	27.6%	24.4%	13.0%		
Manic hospitalizations (US)	650	53.9%	17.4%	18.3%	10.5%	20.0	0.00
Manic hospitalizations (Europe)	279	38.7%	19.4%	25.8%	16.1%		