

Brief Reports

Rapid Cycling in Women and Men With Bipolar Manic-Depressive Disorders

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Objective: This study investigated risks for rapid cycling, as defined by DSM-IV, in women and men with bipolar disorders. **Method:** The results of 10 studies with a total of 2,057 bipolar patients were meta-analyzed by pooled contingency methods. **Results:** The proportions of women and men among rapid-cycling cases averaged 72% and 28%, respectively, but the risk of rapid cycling was inconsistently more frequent among women (29.6%) than among men (16.5%). The mean number of episodes per year was much higher in rapid-cycling patients before and during lithium treatment but was similar in rapid-cycling men and women. **Conclusions:** Rapid cycling was only moderately, and inconsistently, more common in bipolar women than men.

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A rapid-cycling course (1, 2), with at least four major affective episodes in a year, is included in DSM-IV as a diagnostic specifier for the criteria for bipolar manic-depressive disorders. Rapid cycling appears to be a diagnostically reliable phenomenon (3–5), is particularly common among patients with type II bipolar disorders, is associated with high rates of morbidity with potentially severe disability, and may predict an unsatisfactory response to lithium maintenance treatment (6–10). The reported incidence of rapid-cycling patients among persons with bipolar disorders is about 15%, although this rate may be somewhat inflated because of sampling from specialized mood disorders

clinics where such difficult patients may be overrepresented (1–10).

It is widely accepted that women with a bipolar disorder are at particularly high risk of rapid cycling (6, 7). Women have accounted for 72.6% (range=58%–92%) of rapid-cycling bipolar patients (9, 10). However, these rates do not necessarily represent the sex-specific risk of a rapid-cycling course, since clinical samples may contain dissimilar proportions of women and men at risk. In an attempt to clarify this remaining uncertainty, we evaluated the relative risk of rapid cycling in women and men with a bipolar disorder.

METHOD

Reports containing data on the sex distribution of patients with rapid-cycling (four or more episodes in a year) and non-rapid-cycling bipolar disorder were located by means of a computerized literature search (MEDLINE) supplemented by previous reports (1–10) and their citations. The studies that were included in this analysis provided data to permit specific comparisons of rates of rapid cycling in bipolar women and men. To the nine reports that were found we added new data on 355 patients with bipolar disorder from the Lucio Bini mood disorders research center in Cagliari, Sardinia, evaluated as described previously (11). Sex distribution was analyzed by comparing rates of rapid-cycling cases in women and men within, across, and between studies by Mantel-Haenszel (chi-square) methods for pooling contingency tables in meta-analyses (12, 13).

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TABLE 1. Rapid Cycling in Women and Men With Bipolar Disorders in 10 Studies

Study	Year	Number of Subjects					Rapid-Cycling Patients ^a						Risk of Rapid Cycling ^b		
			Women		Men		Total		Women		Men		Ratio (W/M)	χ^2 (df=9)	p
			N	%	N	%	N	%	N	%	N	%			
Dunner et al. (1) ^c	1977	306	151	49.3	155	50.7	40	13.1	28	18.5	12	7.7	2.39	7.85	0.009
Kukopulos et al. (2) ^d	1980	434	256	59.0	178	41.0	87	20.0	61	23.8	26	14.6	1.63	5.57	0.03
Cowdry et al. (14) ^e	1983	43	30	69.8	13	30.2	24	55.8	20	66.7	4	30.8	2.17	3.40	0.07
Joffe et al. (15) ^e	1988	42	27	64.3	15	35.7	17	40.5	7	25.9	10	66.7	0.39	5.06	0.02
Nurnberger et al. (16) ^e	1988	195	113	57.9	82	42.1	29	14.9	25	22.1	4	4.9	4.53	9.84	0.002
Coryell et al. (3) ^e	1992	243	130	53.5	113	46.5	45	18.5	32	24.6	13	11.5	2.14	6.89	0.01
Lish et al. (17) ^f	1993	89	65	73.0	24	27.0	45	50.6	37	56.9	8	33.3	1.71	3.02	0.08
Bauer et al. (4) ^g	1994	239	144	60.3	95	39.7	120	50.2	84	58.3	36	37.9	1.56	9.56	0.003
Maj et al. (5) ^e	1994	111	62	55.9	49	44.1	37	33.3	24	38.7	13	26.5	1.46	1.83	0.25
Current study ^g	1998	355	227	63.9	128	36.1	54	15.2	39	17.2	15	11.7	1.47	1.89	0.22
Total		2,057	1,205	58.6	852	41.4	498	24.2	357	29.6	141	16.5	1.79	59.5	<0.0001

^a Four or more episodes per year.^b Mantel-Haenszel pooled contingency analysis.^c Feighner criteria.^d ICD-9 criteria.^e Research Diagnostic Criteria.^f DSM-III-R criteria.^g DSM-IV criteria.

RESULTS

A total of 10 studies (1–5, 14–17) with 2,057 bipolar disorder patients provided suitable data (table 1). There were more female subjects than male subjects, with no evidence of sex bias in case selection. A rapid-cycling course was found in 24.2% of the patients, but this rate was probably inflated by selection of rapid-cycling cases in some studies (4, 14, 15, 17) that had unusually high proportions of such cases (40.5%–55.8%). Women and men, respectively, represented 71.7% (357/498) and 28.3% (141/498) of rapid-cycling cases (a 2.53-fold difference), but rapid cycling occurred in only 29.6% of women and 16.6% of men. This 1.78-fold difference was statistically highly significant when all available data were pooled. However, significant sex differences in the risk of a rapid-cycling course were found in only six of the 10 studies (table 1), and there was highly significant inconsistency of results across studies (for lack of homogeneity, $\chi^2=40.2$, df=9, $p<0.0001$).

Among our own unselected bipolar subjects, 15.2% had rapid cycling. The cycling rate (episodes per year) before maintenance treatment was 2.52 times higher among the 54 rapid-cycling patients (mean=3.85, SD=3.78) than among the 301 non-rapid-cycling patients (mean=1.53, SD=1.61) ($t=7.42$, df=353, $p<0.0001$). The rapid-cycling patients also had a 2.17 times higher average cycling rate during lithium maintenance treatment (mean=1.38, SD=1.99, versus mean=0.63, SD=0.70; $t=4.54$, df=353, $p<0.001$). However, there was little difference in cycling rates between the 15 rapid-cycling men and the 39 rapid-cycling women before lithium maintenance treatment (mean=4.94, SD=4.58, and mean=3.41, SD=3.38, respectively; $t=1.33$, df=52, n.s.) or during lithium maintenance treatment (mean=1.21, SD=2.37, and mean=1.45, SD=1.85, respectively; $t=0.39$, df=52, n.s.).

DISCUSSION

This analysis included all of the studies we found that had data permitting computation of rates of rapid cycling in bipolar women and bipolar men. It was limited by variance in patient selection and diagnoses and possible underreporting of rapid-cycling men, given a widespread impression that rapid cycling is much more common in women (1–10). More women than men (2.53-fold) were found among the rapid-cycling bipolar patients. However, the sex difference favoring women was inconsistent (six of 10 studies) and more moderate (1.79-fold) than suggested by analyses based on the frequency of women and men among rapid-cycling bipolar patients (1–10). Moreover, cycling rates (average number of episodes per year) were similar in rapid-cycling men and women both before and during lithium maintenance treatment.

Evidently, estimates of risk based on the proportion of women among rapid-cycling patients can be misleading, perhaps because of sampling factors, including possible overrepresentation of women among patients treated for major mood disorders. Although the reported sex ratio of risk for bipolar disorders is close to 1.0 (7, 18), women may more often seek and accept treatment for major mood disorders, including lithium for bipolar disorders (7) and antidepressants for non-bipolar major depression (19). In turn, some of the risk for rapid cycling in women may reflect excessive use of antidepressants without adequate mood-stabilizing treatment (2, 4, 7, 20). In conclusion, the present findings indicate that rapid cycling in bipolar disorders occurs in both men and women, with somewhat greater risk in women, but at similar cycling rates before and during lithium maintenance treatment in both sexes.

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