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Brief report

15-year outcome of treated bipolar disorder

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Abstract

Background: Prior reports suggested that bipolar patients in Taiwan had comparable long-term outcome to Western patients despite markedly lower rates of co-occurring substance use disorders. Thus, predictors of long-term outcome identified from Taiwanese bipolar samples may be less influenced by substance abuse. *Methods*: One hundred and one patients with bipolar disorder (DSM-III-R) having been naturalistically treated for at least 15 years were recruited. These patients were annually followed for 2 years to assess overall outcome, psychiatric symptoms, rehospitalization, work, and social adjustment. A combination of medical record reviews and direct personal interviews with patients and family members provided the clinical data. *Results:* Of these patients, 16.8% expressed a poor overall long-term outcome, even though only two (2.0%) patients exhibited alcohol dependence during the follow-up period. Multivariate regression showed that full compliance with medication was the strongest predictor of favorable overall long-term outcome, followed by younger age at onset and male sex. Younger age at onset as well as male sex, but not full compliance, also predicted a favorable psychosocial outcome. *Limitations:* Recruiting our sample from a clinical population with uncontrollable long-term treatment limits the generalizability of the findings. *Conclusions:* Compliance with pharmacotherapy is important to achieve a favorable overall long-term outcome of bipolar disorder. A portion of bipolar patients may have an unfavorable psychosocial outcome regardless of the psychopharmacological intervention or presence of substance abuse.

Keywords: Bipolar disorder; Predictor of long-term outcome; Psychosocial intervention; Compliance

1. Introduction

In recent years, several studies have suggested that a substantial portion of bipolar patients experience unfavorable psychosocial outcomes and clinical

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course (Coryell et al., 1998; Strakowski et al., 1998), despite the increasing availability of effective pharmacologic treatments (Gitlin et al., 1995). Identifying which patients are at risk for poor outcome remains difficult since specific outcome predictors in bipolar patients receiving modern treatment are incompletely defined (Coryell et al., 1998; Strakowski et al., 1998).

The existing reports concerning predictors of outcome in bipolar disorder all involve studies of Western patients. In these Western samples, bipolar outcome is complicated by high rates of co-occurring alcohol and drug use disorders, making it difficult to identify other environmental factors and other disease characteristics associated with outcome (Goodwin and Jamison, 1990; Brady and Lydiard, 1992). Co-occurring alcohol and drug use disorders appear to indirectly and directly worsen the outcome of bipolar disorder (Feinman and Dunner, 1996; Strakowski et al., 1998). Therefore, in Western samples, the high co-occurrence of bipolar and substance use disorders obscures the specificity of the outcome predictors for bipolar disorder.

In Taiwan, fewer than 10% of bipolar patients also abuse drugs and alcohol (Tsai et al., 1996, 1997; Lin et al., 1998). We previously demonstrated that, despite this difference in rates of substance use disorders, the long-term psychosocial outcome in marriage, work, and social adjustment is comparable to that of Western patients (Tsai et al., 1997). Therefore, in patient samples from Taiwan, we may be able to identify predictors of long-term outcome that are less influenced by alcohol and drug abuse, which was the goal of the current study.

2. Methods

The bipolar patients for this report participated in an outcome study which was initiated in 1995 at the Taipei City Psychiatric Center, Taiwan (TCPC). The TCPC is a 300-acute-bed psychiatric teaching hospital which serves the Taipei Metropolitan area. Originally, 158 patients with bipolar disorder (DSM-III-R, American Psychiatric Association, APA, 1987) were identified from a careful review of medical records according to the following criteria: (1) the patient had been treated for more than 15 years from the first contact at TCPC and (2) the patient had at least 30 follow-up visits at the TCPC. These identified patients were then contacted for possible participation in our outcome study.

The methodology as well as the interview instrument, the Psychiatrist Diagnostic Assessment (PDA), which was used to determine the Axis I diagnosis has been described extensively elsewhere (Tsai et al., 1997). There were 101 (63.9%) patients who provided written informed consent and agreed to participate in this study. National identity numbers were used to search for deceased subjects among the original 158 possible study participants, and ten patients had died prior to our evaluation. The main reason why the other 47 original subjects were unavailable for research interviews was that they could not be located due to changes in address and telephone number. The 101 patients in this study were annually contacted through personal or telephone interview for follow-up evaluations, whether or not they continued to receive treatment through the TCPC.

Sociodemographic and clinical data were collected from medical records, and direct interviews of the patients and their family members. So that our results could be compared to previous naturalistic studies (Harrow et al., 1990; Goldberg et al., 1995), we used the Strauss–Carpenter scales (Strauss and Carpenter, 1972) and the LKP scale (Levenstein et al., 1966). The annual semi-structured follow-up evaluations were conducted by the authors (S.Y.T., J.C.L.) who had achieved satisfactory interrater reliability on the LKP and Strauss–Carpenter scales for individual items, intraclass correlation coefficient, ICC = 0.74–0.98). The eight-point LKP Scale was divided into three broad outcome categories, designated as good functioning (scores of 1 or 2), fair (i.e., moderate impairment; scores of 3–6), and poor overall functioning (scores of 7 or 8). Specific areas of functioning were rated by the Strauss–Carpenter scales including psychiatric symptoms, rehospitalization, work, and social adjustment.

Social class was rated according to the Hollingshead–Redlich Index of Social Position (Hollingshead and Redlich, 1958). Full compliance was defined as 75–100% adherence to the prescribed medication treatment regimen (Keck et al., 1998)

and was determined through the reports of patients and family members. Significant physical illness was recorded if it was potentially life threatening and the patient was not receiving regular medical care.

The univariate linear regression was used for univariate analyses. With the psychopathological and psychosocial scores of the Strauss–Carpenter scales as the dependent variable, the relevant variables at the last follow-up assessment found to be significant in univariate analysis were entered into a multivariate regression to identify outcome predictors while controlling for interactions among the variables. To include the nominal variables in the multiple regression, dummy coding was used for categorical variables.

3. Results

The original sample, identified from review of medical records, consisted of 60 (38.0%) men and 98 (62.0%) women (mean age = 45.3±10.7 years). The demographic data of the original sample from medical records at the last hospital visit showed that 64 patients (40.5%) were unmarried or divorced, 68 patients (43.0%) had less than 9 years of education, and 112 patients (70.9%) were rated in the lower socioeconomic classes (Hollingshead's class IV or V). In the 101 probands, 82 (81.1%) patients were rated as lower socioeconomic classes. Other sociodemographic and clinical variables from the last research interview in 101 patients are presented in Table 1 and did not significantly differ from those of the original sample. None of the 101 patients dropped out or died in the 2 years following the initial evaluation. There were two women and eight men (9.9%) with a life-time diagnosis of alcohol use disorders, but only two men remained alcoholic and met the diagnosis of alcohol use disorders at the time of the last research interview. Although, there has been a dramatic increase in methamphetamine and heroin abuse in Taiwan since the late 1980s (Chen et al., 1999), none of these subjects reported histories of abusing these substances. Additionally, no other drug abuse occurred in these patients. According to the LKP scale, 48 patients (47.5%) had a good overall outcome, 36 (35.6%) a fair outcome, and 17 (16.8%) a poor outcome.

Table 1 displays the results of univariate analyses. Age at onset ($\beta = -0.28$, $t = -2.91$, $P < 0.005$) and male sex ($\beta = 0.20$, $t = 2.13$, $P < 0.05$) emerged as significant predictors of psychosocial scores (work

Table 1
Clinical variables of 101 bipolar patients related to psychopathological and psychosocial scores of the Strauss–Carpenter scales: univariate linear regression

	Mean (S.D.)	Psychopathological scores		Psychosocial scores	
		P	Coefficient	*P*	Coefficient
Continuous variable					
Current age	47.2(10.7)	0.06	–	< 0.01	− 0.264
Age at onset	22.5(8.0)	0.28	–	< 0.005	− 0.286
Number of prior affective episodes	9.2(9.8)	0.07	–	0.05	− 0.196
Years of lithium treatment	10.8(5.7)	0.09	–	0.06	0.190
Categorical variable	*N* (%)				
Marital status		0.27	–	0.26	–
Never married	24(23.8)				
Married	65(64.4)				
Separated or divorced	11(10.9)				
Male sex	38(37.6)	0.37	–	< 0.05	0.215
Lifetime comorbid alcohol abuse	10(9.9)	0.22	–	0.11	–
Rapid cycling(≥ four episodes in a year)	22(21.8)	0.70	–	0.77	–
Prior hospitalization for major depression	38(37.6)	0.05	− 0.221	0.28	–
Significant physical comorbidity	53(52.4)	0.09	–	0.12	–
History of psychotic symptoms	59(58.4)	0.69	–	0.96	–
Full compliance with treatment	67(66.3)	< 0.001	0.377	0.16	–

and social adjustment) in the Strauss–Carpenter scales ($P < 0.04$). This standard method yielded multiple $R = 0.35$, predicting 12.3% of the variance of the psychosocial scores of Strauss–Carpenter scales ($P < 0.04$). Younger age at onset and male sex may predict better psychosocial outcome. In terms of psychopathological outcome (psychiatric symptoms and rehospitalization), only full compliance with medication ($\beta = 0.35$, $t = 3.76$, $P < 0.001$) emerged as a significant predictor and explained 13.3% of the variance in psychopathological scores in the Strauss–Carpenter scales. Full compliance with medication, younger age at onset, and male sex emerged as significant predictors of total Strauss–Carpenter scales scores. Full compliance with medication ($\beta = 0.27$, $t = 2.81$, $P < 0.008$) contributed the most (7%) to the variance of total Strauss–Carpenter scales scores, followed by age at onset ($\beta = -0.26$, $t = -2.71$, $P < 0.01$) and male sex ($\beta = 0.20$, $t = 2.04$, $P < 0.05$). Together, the three variables accounted for 15.8% of the total variance of the Strauss–Carpenter scales ($P < 0.05$). Full compliance with medication, earlier age at onset, and male sex may predict favorable overall outcome.

4. Discussion

Based on the LKP Scale, 16.8% of bipolar patients were rated as having a poor overall long-term outcome, compared to 17–34% with following up less than 4.5 years in previous studies using this measure (Harrow et al., 1990; Goldberg et al., 1995). Furthermore, our results are consistent with the approximately 20% poor long-term outcome with symptomatic and functioning measurements in other naturalistic studies (O'Connell et al., 1991; Coryell et al., 1998). Thus, the general outcome of these Taiwanese patients resembles Western samples.

Although only 9.9% of these patients exhibited a lifetime history of alcohol use disorders, the decrease in alcohol abuse over the 15-year period of treatment is consistent with reports from Winokur et al. (1995) and strengthens the ability of this study to identify outcome predictors of bipolar disorder independent of substance abuse. We found that full compliance with medication was the strongest predictor of favorable overall long-term outcome. These findings are consistent with prior studies of predictors of outcome (Strakowski et al., 1998; Keck et al., 1998). Younger age at onset and male sex, but not full compliance with medication, were associated with a favorable psychosocial outcome as well. However, it should be noted that these variables explained only a small portion of the total variance, suggesting other factors that we did not measure significantly impacted the outcome of these bipolar patients.

In our analysis, full compliance with medication was not associated with psychosocial outcome. One explanation for this observation is that independent factors become important for different aspects of recovery, as suggested by others (Harrow et al., 1990; Goldberg et al., 1995). Strakowski et al. (1998) previously observed that full treatment compliance may be sufficient to initiate syndromic recovery, yet psychosicoal rehabilitation may be necessary for functional recovery. Thus, our results support the hypothesis that pharmacotherapy alone is not fully effective in enhancing long-term psychosocial outcome.

Age at onset has been included in many studies as a potential correlate of outcome but has often either not proven useful as a predictor of outcome in general or has been associated with worse outcome (Coryell et al., 1998). However, we have previously shown that an earlier age of onset correlates with suicidal behavior in bipolar disorder in Taiwan (Tsai et al., 1999). Therefore, early-onset bipolar patients with poor outcome might be under-represented in outcome studies due to suicide at a young age prior to being identified for outcome studies. Nonetheless, our finding supports McGlashan's (1988) observation that the 15-year outcome of adolescent-onset bipolar patients is comparable to or better than that of adult-onset patients.

Male bipolar patients are vulnerable to substance abuse along with treatment noncompliance (Goodwin and Jamison, 1990) and are prone to have poor psychosocial outcome (Tohen et al., 1990). In this study, the female patients were found to have both overall and psychosical unfavorable long-term outcomes. This finding could be further evidence of the longitudinal approach to support the idea that bipolar women tend to experience worse prognosis and poor response to prophylactic lithium treatment (Aagaard and Vestergaard, 1990; Leibenluft, 1996). However,

in Western samples, male patients may exhibit worse outcome (Tohen et al., 1990). This difference from previous Western studies could also reflect cultural differences in how men and women with bipolar disorder fare in their respective societies. Clearly, gender difference in long-term outcome remains open for further investigation.

Our findings should be interpreted cautiously due to some methodological shortcomings. First, the requirement of a 15-year naturalistic treatment biased our subjects toward patients who are available for a follow-up study and whose courses featured more persistent symptoms. Thus, the generalizability of our findings is limited to first-episode or community samples. However, the characteristics of our subjects might better represent the typical clinical condition of patients with long-term treatment. Another limitation is that certain important predictors of outcome were not examined, such as persistence of depressive symptoms (Gitlin et al., 1995; Coryell et al., 1998) and premorbid function (Strakowski et al., 1998). As noted, only a small portion of the overall variance in outcome was explained by the variables we identified as significant outcome predictors. Large patient samples might permit a more exhaustive evaluation of the relationships among clinical and demographic variables and illness course in bipolar disorder. Despite these limitations, this is the first study of a non-Western bipolar sample that examined variables associated with long-term outcome.

In summary, full compliance with pharmacotherapy is essential for achieving favorable overall long-term outcome. Despite a marked difference in co-occurring alcohol and drug use disorders between Taiwanese and Western bipolar samples, the quality of outcome and associated predictors are strikingly similar. As substance use disorder is one important factor for unfavorable outcome in Western samples, this study highlights the value of cross-cultural studies of bipolar disorder to explore common outcome predictors.

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