Life Events Precipitating Mania

SIDNEY KENNEDY, RUTH THOMPSON, HARVEY C. STANCER, ALEC ROY and EMMANUEL PERSAD

Summary: A study of 20 manic patients, with patient and matched control comparisons, showed a two fold increase in life events during the 4 month period before admission to hospital. Life events, independent of affective illness and having significant objective negative impact (i.e. traumatic) were significantly more common. These findings are considered in relation to social relationships, family history of affective illness and the use of psychotropic medication.

The relationship between life events and psychiatric disorder has been studied extensively in the past decade (Dohrenwend and Dohrenwend, 1974). Paykel et al (1969) found that depressed patients reported three times as many life events as a control group in the six months before the onset of a depressive episode; in particular, there were significant increases in life events categorized as exits from the immediate social field of the subject and in events categorized as undesirable. Brown and Harris (1978) also reported a significant increase in life events in depressed women, suggesting that the social environment plays a crucial role in the aetiology of depression. While Tennant et al (1981) have criticized the evidence for a substantial causal relation between life events and depressive disorder, Lloyd (1980) concluded that "life events play a precipitating role in the development of depressive disorder."

In contrast to the considerable interest in life events as precipitants of depression, only a few studies have reported on the role of life events as precipitants of mania. Previous studies, with one exception (Hall et al, 1977), are retrospective. Dunner et al (1979) and Patrick et al (1978) reported that 60 per cent of manic patients experienced life events in the three month period preceding onset; men more often than women, with work and interpersonal difficulties most often reported. In a controlled study, using the Social Readjustment Scale of Holmes and Rahe (1967), Glassner et al (1979) found a significant increase in life events resulting in role loss among working class manic-depressive patients but failed to state whether relapses were manic or depressive. Ambelas (1979) reviewed charts of 67 manic patients. In the four week period preceding admission he reported a significant increase in independent life events for 28 per cent of manic patients compared to 7 per cent of 67 surgical controls. In 36 per cent of the manic patients reporting life events a bereavement was noted. In an uncontrolled epidemiological comparison of Danish and English manic patients Left et al (1976) parenthetically noted the presence of an independent life event in the month before the onset of mania in 28 per cent and 29 per cent, respectively. The only prospective study (Hall et al, 1977) reported "a significantly higher frequency of life events relating to employment" in the group of bipolar patients who relapsed with mania during the ten month follow-up period compared with an unmatched bipolar group who did not relapse. The present study reports on life events as possible precipitants of mania. The results are also considered in relation to data on social relationships, parental loss, psychotropic medication and family history of affective disorder.

The hypothesis tested was that manic patients experience a significant increase in independent life events during the four month period preceding the onset of a manic episode when compared to a control group and also when compared to themselves over a subsequent four month period.

Subjects and Method
A consecutive series of 20 manic patients admitted to the Affective Disorders Unit, Clarke Institute of Psychiatry, Toronto, between July 1, 1979 and December 31, 1980 were studied. All patients were evaluated by two psychiatrists (H.C.S. and E.P.) and met Feighner et al, criteria (1972) for primary bipolar affective disorder-mania, following administration of the Renard Diagnostic Interview (Helzer et al, 1981). An additional inclusion criterion was a minimum period of 6 months without in-patient care for either
depression or mania both before and after the index admission. Subjects were contacted by letter and asked to attend an interview to provide information not previously covered at the time of their admissions. Written informed consent was obtained from all patients who were interviewed at least six months and not longer than 21 months after discharge, at a time when they were assessed to be euthymic. Each manic patient was matched for age (within 5 years), sex, marital status, social class and whether Canadian or foreign born, with the next orthopaedic outpatient attending a sports medicine clinic. Prospective controls were also given a letter asking if they would provide information not related to their present injury. They then completed the General Health Questionnaire, 30 item version, (Goldberg, 1972) with a cut off score of 9 as recommended by Finlay-Jones and Murphy (1979) for use in patients with physical disorder. They were also given a brief psychiatric interview to exclude present or past psychiatric disorder. Goldthorpe and Hope’s (1974) classification of occupations was used to determine social class; 1–22 were called middle class and 23–36 working class.

At interview each bipolar patient was asked about life events during the 4 month period before admission to hospital, and also during a 4 month period starting 2 months after discharge from hospital. (This was to allow for the effects of discharge from hospital—a significant life event in itself.) Each control was asked about life events during the temporally identical period which preceded the admission for mania of the patient with whom he was matched. Paykel et al’s, 64 item revised Recent Life Events Interview (1980) was used to obtain details of changes in work, education, finances, health, bereavement, residence, legal issues, family and marital situation and an additional open ended question to include any other areas not specifically covered. Interviews were carried out on subjects and controls by two of us (S.K. and R.T.): the first ten being done jointly and scored independently with high inter-rater reliability being obtained. All events were enquired about with detailed questioning on each positive response to establish the exact time and full circumstances of the event. For each event two additional ratings were made (by R.T. and S.K.), after each interview was completed. These were (1) ‘Objective negative impact: a modification of Brown’s contextual threat (Brown and Harris, 1978) which measured on a 1–5 scale the adverse effect such an event would have on an individual given all the circumstances, but ignoring the subjective reporting of impact; (2) ‘Independence’. Also on a 1–5 scale, this rated the likelihood that the event was not a consequence of mania or depression. Manic patients and orthopaedic controls were also asked about social relationships during the matched time periods, using a modification of the questionnaire used by Brown and Harris (1978) to establish the presence or absence of a confidant. Details about the family history of psychiatric illness (using Feighner criteria) were available for the manic patients from independent family interviews conducted by trained interviewers in connection with a separate family study (Weitkamp et al, 1981). Information about parental loss was also obtained from the interview. In addition information was collected about drug treatment of the manic patients by both interview with the patients and a review of the hospital charts. Drug dosage and blood levels, where available, were recorded for the 4 month periods before and after admission.

Results

Both groups contained 14 women and 6 men. For the manic patients the mean age was 38.9 years (SD±14.8) and for the orthopaedic controls 38.5 years (SD±14.3). Nine of the patients in both groups were single, 8 were married and 3 were separated or divorced. Seventeen of the patients in both groups were middle class and 3 were working class. The mean age for the first episode of bipolar affective disorder among the manic patients was 30.9 (SD±13.0) and the mean number of psychiatric admissions for affective disorder was 4.3 (SD±4.5). For 4 of the women and 1 man this manic illness was the first episode of affective disorder. In 17 of the 20 manic patients, at least one family member was diagnosed (according to Feighner criteria) as having a history of affective disorder. The mean score on the GHQ for the control patients was 2.3 (SD±2.9, range 0 to 9).

Life events were compared in the 20 manic patients before and after hospital admission (Table 1). Seventeen (85 per cent) experienced one or more life events (total 46 events, mean 2.3, SD±1.62) during the 4 month period before admission, while fourteen (70 per cent) experienced one or more life events (total 27 events, mean 1.35, SD±1.03) during the 4 month period after discharge from hospital (t value = 2.83, df 38, P <0.01). When independent events were compared, 23 of 29 (79.3 per cent) were rated as having severe, marked or moderate objective negative impact in the 4 months before admission compared to 7 of 21 (33.3 per cent) in the 4 months after discharge (t value = 3.56, df 38, P <0.002). Thirty of the 46 life events (65.2 per cent) in the 4 months before admission to hospital were undesirable events compared with 11 of the 27 (40.7 per cent) in the 4 months after discharge (t value = 4.05, df 38, P <0.001). There was no significant difference, however, in events rated as desirable (2 versus 3). Comparisons of events involving the entrance (3 versus 0) or exit (5 versus 1) of an
individual from the patient's social field also showed no significant difference.

The second set of comparisons was between the 20 manic patients before admission and the 20 control patients (Table II). Twenty five life events were reported by 15 of the 20 control subjects (mean 1.25, SD ± 1.03) compared to 46 life events by 17 manic patients (85 per cent). These differences were significant (mean 2.3, SD = 1.62, t value = 2.32, df 38, P <0.02). Undesirable events were also significantly more common among manic patients: 30 of 46 (65.2 per cent), compared to 8 of 25 (32 per cent) among control subjects (t value = 4.06, df 38, P <0.001). Comparisons of desirable events (2 versus 3) and entrance (3 versus 3) or exit (5 versus 1) events again showed no significant differences.

Further comparison of events according to area of activity showed a significant difference in employment related events. Eleven manic patients and 13 control subjects were in full time employment during the period of the study. Twelve patients experienced 14 employment related events before admission; eight patients experienced nine employment related events after discharge and four controls experienced five such events. Only the difference between manic patients before admission to hospital and control subjects was significant (t value = 2.35, df 38, P <0.02).

A social relationship rating of adequate (based on the presence of a confidant) was made in 6 manic patients before admission, in 11 manic patients after discharge, and in 14 of the control subjects. The difference between manic patients before and after admission was not statistically significant, but the difference between manic patients before admission and control subjects was significant (t value = 2.08, df 38, P <0.05). All subjects rated as having an adequate confiding relationship (both manic patients before admission to hospital and control subjects) were compared to all subjects rated as having an inadequate confiding relationship. There was a significant increase in undesirable events among those who did not have a confiding relationship (t value = 2.15, df 38, P <0.04).

No significant differences were found between manic patients and control subjects for early parental loss; in 2 manic patients and 3 controls a parent had died before the patient was 11 years of age while 7

### Table I

<table>
<thead>
<tr>
<th>Life events</th>
<th>4 months before episode</th>
<th>4 months after episode</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Independent with severe, marked or moderate objective negative impact</td>
<td>23</td>
<td>7</td>
<td>&lt;0.002</td>
</tr>
<tr>
<td>Independent with mild or no objective negative impact</td>
<td>6</td>
<td>14</td>
<td>NS</td>
</tr>
<tr>
<td>Undesirable</td>
<td>30</td>
<td>11</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Desirable</td>
<td>2</td>
<td>3</td>
<td>NS</td>
</tr>
<tr>
<td>Exit</td>
<td>5</td>
<td>1</td>
<td>NS</td>
</tr>
<tr>
<td>Entrances</td>
<td>3</td>
<td>0</td>
<td>NS</td>
</tr>
<tr>
<td>Total</td>
<td>46</td>
<td>27</td>
<td>&lt;0.02</td>
</tr>
</tbody>
</table>

### Table II

<table>
<thead>
<tr>
<th>Life events</th>
<th>Manic patients 4 months before episode</th>
<th>Controls during same 4 month period</th>
<th>Significance</th>
</tr>
</thead>
<tbody>
<tr>
<td>Undesirable</td>
<td>30</td>
<td>8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Desirable</td>
<td>2</td>
<td>3</td>
<td>NS</td>
</tr>
<tr>
<td>Exits</td>
<td>5</td>
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<td>Entrances</td>
<td>3</td>
<td>3</td>
<td>NS</td>
</tr>
<tr>
<td>Total</td>
<td>46</td>
<td>25</td>
<td>&lt;0.02</td>
</tr>
</tbody>
</table>
manic patients and 3 controls had experienced separation for more than 1 year from one or both parents before they were 11 years of age.

During the 4 month period before admission to hospital, 6 of the 15 manic patients (40 per cent) with previously diagnosed and treated affective disorder were receiving lithium carbonate consistently over that time with blood levels above 0.6 mEq/l (mean 0.9, SD±0.3). One patient was receiving antidepressant drugs in the 4 months before admission compared to 3 in the 4 months after discharge. Neuroleptic drugs were prescribed for 3 patients before admission and 4 patients after discharge. None of these differences was statistically significant.

Finally, comparisons were carried out according to sex and whether or not the manic episode studied was the beginning of a previously undiagnosed bipolar affective disorder. No significant differences could be demonstrated with respect to any of the variables previously considered.

**Discussion**

The evidence for biological factors in bipolar affective illness is strong (Shopsin, 1979). By using both non patient and between patient controlled comparisons, the possibility that manic patients would experience excessive life events independently of mood state was considered and found not to be the case.

Manic patients experienced twice as many life events before admission to hospital as control subjects, or as compared to themselves during a similar period after discharge from hospital. Events rated as independent of affective illness and having moderate, marked or severe objective negative impact were three times more prevalent in manic patients before admission than after discharge. Significantly fewer manic patients had a confiding relationship before admission compared to controls. The perceived increase in confiding relationships among manic patients after discharge, although not significant, is surprising in view of the considered enduring nature of such a relationship (Brown and Harris, 1978). This may be explained to some extent by the determined effort made by both patients and relatives after a period of in-patient care to improve mutual understanding.

Several problems are inherent in this type of retrospective study. The tendency to search for explanations had been called 'the effort after meaning' (Bartlet, 1932) and has been claimed to occur in depressed patients (Lipman et al, 1965). However our patients were not admitted for depression during the periods studied and were only interviewed at a time when they were euthymic. An increase in the occurrence of life events preceding hospital attendance for non-psychiatric illness has been reported (Holmes and Masuda, 1974) so that the differences reported here between manic patients and controls become all the more striking. Because distortion of recall over time has also been reported (Jenkins et al, 1979) manic patients and controls were individually matched in this study for time of recall. The issue in life event research of interviewing a relative is controversial (Hudgens et al, 1970) but Brown et al (1973) have shown an agreement in the recall of life events of about 80 per cent between patients and additional informants. There is usually a short time period between onset of manic symptoms and admission to hospital. This means that the dating of symptom onset of the manic illness is likely to be more precise, and helps in separating those events rated as independent preceding the onset of illness.

To the best of our knowledge the present report is the only matched controlled study of manic patients where life events, social relationships, family history of affective illness and the use of psychotropic medication were all considered. Care was also taken to minimize the effects of a previous manic or depressive episode by ensuring that patients studied were free of any psychiatric illness for 6 months before and after admission.

The lower incidence of life events as reported by Ambelas (1979), where 28 per cent of manic patients were noted to have experienced a life event in the 4 week period prior to admission may be due to the shorter time period he studied (compared to the 4 months of this study) and also due to the reliance on retrospective chart material to assess life events. Dunner et al's (1979) study considered a 3 month period prior to onset of mania and they found 57 per cent of manic patients reported a significant life event before onset, (compared to 85 per cent) in the 4 month period before admission to our study. Events covered in their questionnaire fell into similar categories to those used here. As in this study, Dunner et al, found a significant occurrence of work-related problems among 20 per cent of his patients. However, their study lacked a control group and also required recall of the first admission, often many years earlier. Hall et al (1977) also recorded a significant occurrence of work related events prior to manic relapse in their prospective study of bipolar patients. In this study also, manic patients experienced more work related events before manic illness than did the control patients.

Previous critics (Andrews et al, 1978) have suggested that events, particularly those involving interpersonal conflict, could be symptomatic of manic or depressive
illness. Where any doubts existed in this study that depression prior to mania or early symptoms of mania could have contributed to the occurrence of the event, a rating of probably or possibly dependent was given, excluding further consideration as an independent event. There was, nevertheless, a significant increase in independent events in the manic group compared to the control group, and no difference between the groups for marital conflict which is also supportive evidence that the manic patients had not become ill with mania during the period in which life events were assessed.

None of the previous studies addressed the question of medication: namely that those with recurrent affective disorder not treated with prophylactic medication would be more at risk for relapse. In this study there was no significant difference in the number of patients receiving prophylactic medication before or after the episode of mania. Exit events have been shown to occur in excess before depressive episodes (Paykel et al., 1969). That finding was not replicated in this study. Thus further investigation of the nature of events before relapse among patients with bipolar affective disorder may be informative. In conclusion, this study suggests that life events may act as precipitants for manic episodes, particularly in the absence of an adequate confiding relationship in some patients with bipolar affective disorder.

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