British Journal of Psychiatry (1993), **162**, 161–166

Review Articles

Stressful Life Events and Schizophrenia
I: A Review of the Research

ROSS M. G. NORMAN and ASHOK K. MALLA

Empirical research concerning the relationship between life event stressors and schizophrenia is critically reviewed. In accordance with the view that patients suffering from schizophrenia are vulnerable to stress, there is evidence of a relationship between stressors and variation in severity of symptoms over time. There is less indication that schizophrenic patients have had higher levels of stressors than the general population or than patients suffering from other psychiatric disorders. These findings are consistent with vulnerability–stress models of the development of schizophrenia.

It is frequently stated in the scientific literature that schizophrenia and its symptoms are influenced by stressful life events (Zubin & Spring, 1977; Nuechterlein & Dawson, 1984*a*; Weinberger, 1987; Boker *et al*, 1989). Many clinicians assume that this assertion is correct. In addition there has been considerable speculation about why schizophrenic patients are likely to be particularly susceptible to the effects of stress (Spring & Coons, 1982; Nuechterlein & Dawson, 1984*b*; Nicholson & Neufeld, 1989). Despite the strength and endurance of the assumption that stress influences schizophrenia, past attempts at a dispassionate review of the literature have generally concluded that the evidence for such a relationship is weak (Rabkin, 1980; Dohrenwend & Egri, 1981; Tennant, 1985).

As Rabkin (1980) noted, when past research in this area is examined, one finds that studies have been providing empirical evidence relevant to three separate issues. Some studies have reported data on whether schizophrenic patients appear to have higher rates of life event stressor than patients who have been given other psychiatric diagnoses. Others have reported on whether schizophrenic patients have more life event stressors than the general population. Finally, there are studies that have examined whether there is a relationship in schizophrenic patients between level of life event stressors and severity of symptoms. There are a few studies (e.g. Brown & Birley, 1968; Chung *et al*, 1986) that provide evidence relevant to more than one of these three issues. Unfortunately, little attention has been paid to the differences between these three issues and the rationale for the questions that they ask. There is actually a much stronger rationale for expecting to find the latter of these three types of relationship than for the other two.

The justification for expecting schizophrenic patients to have higher levels of life event stressors than other diagnostic groups of psychiatric patients is questionable. In order to expect such a difference, we would have to assume that the symptoms of patients with other psychiatric diagnoses are less influenced by stress than are those of schizophrenic patients. This is a difficult assumption to justify, particularly if the comparison is between schizophrenia and depression. There is considerable evidence that although there are probable biological vulnerabilities to depression, there is also a substantial relationship between depressive symptoms and life event stressors (Brown & Harris, 1978; Lloyd, 1980; Paykel, 1982). However, almost all of the studies that have been reported comparing levels of life event stressors in schizophrenics with those in other patients have used depressed patients as the comparison group.

The rationale for expecting to find a strong and reliable difference between schizophrenic patients and normal controls in the level of stress is also problematic. The difficulties with such a prediction can be illustrated by referring to a set of diathesis–stress or vulnerability–stress models that have been proposed (e.g. Meehl, 1962; Rosenthal, 1970; Zubin & Spring, 1977; Gottesman & Shields, 1982; Nuechterlein & Dawson, 1984*a*; Asarnow & Goldstein, 1986; Boker *et al*, 1989). Such models differ in their details, but all assume that people have varying degrees of vulnerability to the development of schizophrenia and that the likelihood of schizophrenic symptoms actually occurring at any point in time is a function of both the extent of the biologically influenced vulnerability and the magnitude of stress that the individual is encountering. The vulnerability approach postulates that there is a trade-off between vulnerability and the amount of stress that can be tolerated before symptoms appear.

The essence of the vulnerability models is illustrated schematically in Fig. 1, which is adapted from Zubin & Spring (1977). Note that the shape of the curve

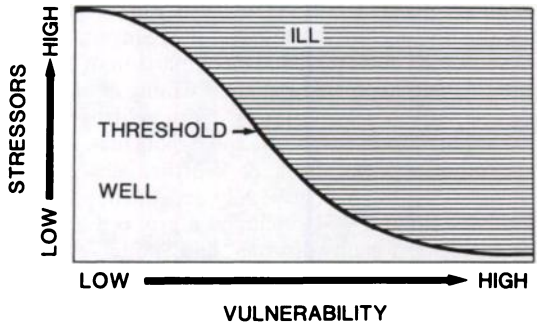

Fig. 1 Proposed relationship between vulnerability and stressors as influences on schizophrenia.

or function relating vulnerability to stress can be seen as representing a compromise between two positions. One position would see vulnerability to schizophrenic symptoms as a dichotomy; either you have it or you do not – perhaps a discrete neuroanatomical lesion or genetic anomaly. The other position would see it as a continuum, rather like height or weight – we all have it to varying extents.

Assuming that objective life event stressors are randomly distributed across a population, then we would expect, on the basis of this model, that most of those who develop schizophrenia will do so as a result of high levels of vulnerability combined with only moderate or low levels of stress. Although some people with symptoms of schizophrenia at any point in time may actually have had low vulnerability and extremely high levels of stressors, they would not represent a large proportion of diagnosed schizophrenics. Indeed, the latter group may be more likely to receive other diagnoses (e.g. brief reactive psychosis, schizophreniform illness) as a result of the extremity of the eliciting circumstances and the possibly briefer duration of their symptoms.

One would not, therefore, expect the average level of antecedent stressors for those who develop schizophrenia to be much higher than for a random sample from the general population. Furthermore, from the vulnerability model one would expect variance in stress levels to be considerable within both a schizophrenic population and a comparison normal group. It is unlikely that researchers would find frequent and reliable differences in levels of prior life event stress between those who have and have not developed schizophrenia, especially when studies that make such comparisons typically use symptomatic samples who have been admitted to hospital (often repeatedly), whose symptoms are quite marked, and for whom there is good agreement as to their diagnosis, as these individuals are likely to represent the extreme right-hand side of Fig. 1. In turn, the normal controls are typically individuals for whom there is no evidence of psychiatric symptoms, and are, therefore, likely to represent the extreme left-hand side of the figure. The further to the extreme left or right are the groups that are being compared, the greater is the difference in vulnerability and the less the anticipated difference in mean level of stress.

There are additional considerations that would lead one to be sceptical of finding differences between these groups on mean level of life event stressors. There is an argument to be made that matching patients and normal controls on socio-economic variables, as is sometimes attempted (e.g. Jacobs & Myers, 1976; Canton & Fraccon, 1985), may also decrease the likelihood of finding differences between them on life stressors. In addition, if many schizophrenics have strong aversive reactions to life stressors, it is quite conceivable that they have adapted their lives to ensure minimum exposure to major stressors. One would expect this on the basis of well established behavioural principles of avoidance learning, and it also fits with a common clinical impression that many schizophrenic patients lead lives that do not include many of the acute, major life events (e.g. marriage, divorce, mortgages, promotions) that challenge others. This is not to deny, however, that those suffering from schizophrenia may have higher levels of some chronic problems, such as loneliness, or financial need.

Where then would one look for evidence of a relationship between life event stressors and symptoms of schizophrenia? The strongest relationship would be expected when looking for a relationship between stress and symptoms in those who are relatively similar in level of vulnerability. One might, for example, expect a significant relationship between stress and symptoms of schizophrenia across a group of people all at high risk of schizophrenia on the basis of biological or psychological markers. One might also expect a relationship between stress and symptom severity across a group of diagnosed schizophrenics. The best way of holding vulnerability constant would, of course, be to use each patient as his or her own control by looking for a relationship between variation in stress and symptoms over time.

The evidence

The vulnerability–stress approach to schizophrenia suggests different degrees of support for a relationship between stress and schizophrenia for the three types of comparisons reported. We have classified the reported studies into three categories on the basis of which particular issue they examine: (a) level of life

https://doi.org/10.1192/bjp.162.2.161 Published online by Cambridge University Press

event stressors in schizophrenic patients in comparison with other psychiatric groups; (b) level of such stressors in patients with schizophrenia in comparison with normal controls; and (c) level of such stressors in schizophrenic patients who vary in their severity of symptoms. For each result we determine whether statistically significant relationships were found. We then contrast the proportion of studies showing statistically significant differences across the three types of comparisons outlined.

The studies on which we report are restricted to those which use at least one comparison group composed solely of diagnosed schizophrenic patients. We have included only those studies in which the investigators made an explicit attempt to exclude from consideration those life events that are themselves likely to have been a result of changes in symptoms. In studies where life events were classified by their likely degree of independence from patients' general behaviour, and analyses given separately for each level of independence, we examined the results for each such level. The use of these criteria means that several studies previously cited as relevant to life event stress and schizophrenia are not included (e.g. Michaux, 1967; Serban, 1975; Harder *et al*, 1980).

Several studies (e.g. Brown & Birley, 1968; Al Khani *et al*, 1986; Chung *et al*, 1986) report findings that are relevant to more than one comparison. In several cases it has been necessary for the current authors to carry out statistical analyses on tables of data, when such tests were not reported by the original authors, or when we have reanalysed the data in order to make the results more directly comparable with other studies. In order to allow for more direct comparison of results, we typically examined the data for the total samples described in each study. In a very few studies (e.g. Al Khani *et al*, 1986) secondary analyses were carried out which showed some differences in patterns for subsamples (e.g. males versus females). There is, however, an insufficient number of studies which undertake comparable subanalyses to allow any estimates of the reliability of such group differences.

As several years have passed since the most recent comprehensive review of the literature in this area, we have included several studies not previously reviewed (e.g. Malzacher *et al*, 1981; Canton & Fraccon, 1985; Hardesty *et al*, 1985; Al Khani *et al*, 1986; Chung *et al*, 1986; Ventura *et al*, 1989; Malla *et al*, 1990).

Schizophrenic patients compared with other psychiatric diagnostic groups

Eight studies are included here (Eisler & Polak, 1971; Beck & Worthen, 1972; Clancy *et al*, 1973; Jacobs *et al*, 1974; Lahniers & White, 1976; Leff & Vaughn, 1980; Chung *et al*, 1986; Skodol & Shrout, 1989). Seven of the eight included a comparison of schizophrenic and depressed patients; Chung *et al* (1986) compared patients suffering from schizophrenia, schizophreniform psychosis, and hypomania. Among the other reports, Beck & Worthen (1972) also included a group of chemically dependent patients; Eisler & Polak (1971) included a group diagnosed as having personality disorder; and Skodol & Shrout (1989) included patients with adjustment and anxiety disorders.

All studies used in-patients and a retrospective design in which measures of stressful life events were collected with reference to a period of time before admission. The measures of life events varied widely, and included questionnaires, interviews, and review of chart notes. The period of time covered by the stress measures varied from a "few weeks" to two years. The sample size for schizophrenic patients varied between 15 and 200. (Tables providing more detailed information on the studies relevant to each of the three comparisons are available from the authors on request; these tables include descriptions of the studies, the measures used, the statistical comparisons carried out, and the statistical significance of the results.)

The eight studies provided the basis for 18 statistical comparisons of the number of life event stressors experienced by patients suffering from schizophrenia in comparison with those experienced by patients with other diagnoses. These comparisons typically contrasted indices of stressors for the period leading up to admission or onset of illness. None of the comparisons provided significant evidence of higher levels of stress for schizophrenic patients. In fact, for 10 out of the 18 comparisons (56%), the other psychiatric groups reported significantly higher levels of stressors.

Schizophrenic patients compared with normal controls

There are seven such studies (Brown & Birley, 1968; Jacobs & Myers, 1976; Schwartz & Myers, 1977*a*; Malzacher *et al*, 1981; Canton & Fraccon, 1985; Al Khani *et al*, 1986; Chung *et al*, 1986). At least five of the seven involved schizophrenic in-patients, for whom life events were retrospectively assessed for periods of time from 3 to 12 months before admission. Al Khani *et al* (1986) recruited their patients from an out-patient clinic, but it appears that they also assessed life stressors retrospectively before the onset, relapse, or exacerbation of symptoms. It is not clear from this report whether such increases in symptoms had always involved admission or how

much time had elapsed between the onset of such a symptom and the time of retrospectively collecting life-event data. Schwartz & Myers' (1977*a*) sample consisted of diagnosed schizophrenic patients who were interviewed two to three years after discharge. In the latter study life events were assessed with respect to the six months before the interview as opposed to a period of time before any increase in symptoms. Measures of life event stressors were either structured interviews or check-lists. Schizophrenic patient sample size varied between 15 and 132.

The studies reviewed provided 14 comparisons of whether schizophrenic patients reported higher levels of life event stressors than did normals. In five of the 14 comparisons (36%), patients indicated significantly higher levels of stressors. For none of the comparisons did the normal samples show higher stressors.

Life event stressors and symptoms within schizophrenics

Eight studies are reviewed here. In six studies (Brown & Birley, 1968; Hardesty *et al*, 1985; Al Khani *et al*, 1986; Day *et al*, 1987; Ventura *et al*, 1989; Malla *et al*, 1990) the contrast is made between life stressors assessed for a period of time (three weeks to three months) immediately before the worsening of symptoms, and levels of stressors for the same people for comparison periods of time that do not immediately precede worsening of symptoms. These comparisons are, therefore, intended to relate variation of symptoms within patients across time to variation in level of life stressors. Three of these six studies (Brown & Birley, 1968; Al Khani *et al*, 1986; Day *et al*, 1987) used retrospective assessment of stressors for periods of time varying between 12 weeks and 12 months immediately before onset of illness. In these studies, contrasts were then carried out to see whether there had been higher levels of stressors in the three weeks immediately before onset than the average per three weeks during four to 12 weeks before onset. Three of these studies – Hardesty *et al* (1985), Ventura *et al* (1989) and Malla *et al* (1990) – are especially noteworthy for being the only studies within the life event stressor and schizophrenia literature to use longitudinal designs with repeated measures of levels of stressors and symptoms to relate changes in stress and symptoms over time. Hardesty *et al* and Malla *et al* assessed life stressors every two weeks over the course of a year. Ventura *et al* (1989) assessed stressor levels every month over a year.

The two other studies included in this category (Leff *et al*, 1973; Schwartz & Myers, 1977*b*) focused on comparisons between schizophrenic patients with symptoms of different severities. Using a retrospective design, Leff *et al* (1973) contrasted antecedent life events between groups of relapsed schizophrenic in-patients and non-relapsed groups. Schwartz & Myers (1977*b*) examined the relationship between recall of life event stressors during the preceding six months and a continuous measure of level of symptoms in a group of schizophrenics living in the community.

Brown & Birley's (1968) sample consisted of schizophrenic in-patients. Day *et al* (1987) appear to have included both in-patients and out-patients in their samples. The other studies in this group seem to have used exclusively out-patients. Life event stressors were measured using structured interviews or review of chart notes, and the length of time covered by these measures varied between two weeks and three months. Sample size varied between 11 and 132. Day *et al* analysed data regarding stress and symptoms for six independent samples from different countries, and we examined results separately for each sample.

Of 30 comparisons relating level of stress to level of symptoms within groups of schizophrenic patients, 23 (77%) yielded statistically significant findings of higher levels of antecedent life event stressors being associated with worse symptoms.

Comparative results

In accordance with our expectations, the highest proportion of significant differences in the expected direction was found for comparisons relating level of stress to level of symptoms within groups of schizophrenic patients (77%). The second highest proportion of positive findings is for the comparison of reported stressors for schizophrenic patients versus normals (36%). As expected, the lowest proportion of supportive findings occurs when we look for a higher rate of stressors in schizophrenic patients than in other groups of psychiatric patients. We have contrasted across the three categories the proportion of comparisons which do and do not provide evidence of higher levels of stress being associated with symptoms of schizophrenia, and there is a significant difference ($\chi^2 = 27.35$, d.f. $= 2$, $P < 0.0001$).

Of course, many of the analyses reported are based on repeated and parallel examinations of the same set of data. A more conservative contrast would be between the number of independent samples for which there is some statistically significant evidence of a relationship between higher levels of life event stress and schizophrenia. None of the eight samples in the first category (schizophrenics v. psychiatric patients) provide evidence of higher levels of stressors

for patients with schizophrenia. There were seven independent samples which contrasted schizophrenic patients with normals, of which three (43%) show evidence of higher levels of stress for schizophrenic patients before worsening or the onset of symptoms in comparison with normal controls. There were 14 such independent samples (including the six independent samples in the Day *et al* (1987) report of the World Health Organization's study) relating stressors to schizophrenic patients' symptoms. Of these, 12 (86%) provide statistically significant evidence of higher levels of stress being associated with worse symptoms among schizophrenics. Again, the differences between groups of comparisons in number of positive findings is significant ($\chi^2 = 15.27$, d.f. $= 2$, $P < 0.001$).

These comparisons do not provide definitive evidence for stress influencing schizophrenic symptoms, nor do they prove the validity of conceiving schizophrenia as a joint function of vulnerability and stress. In *general*, however, there is considerably more evidence for variation in stressors being associated with changes in the course of symptoms for schizophrenic patients than for schizophrenics having been exposed to more external life event stressors than the general population or patients suffering from other psychiatric disorders. This is certainly what one would expect if the vulnerability–stress model were correct.

There is considerable variation in several characteristics of the studies reviewed and one must, therefore, be cautious about drawing conclusions from a comparison of their aggregated results. For instance, a wide variety of life event measures were used. The results did not, however, suggest any systematic relationship between the particular life event measure used and the likelihood of a statistically significant result.

There was also a wide range in the time period used for assessment of stressors. Some of the earliest evidence in the field (Brown & Birley, 1968) suggested that it is particularly important to examine stressors that may have occurred within about three weeks of onset or aggravation of symptoms. While some subsequent studies have made a point of examining approximately this period of time (e.g. Hardesty *et al*, 1985; Al Khani *et al*, 1986; Day *et al*, 1987; Ventura *et al*, 1989), others have used much longer periods as a basis for comparisons (e.g. Leff *et al*, 1973; Jacobs & Myers, 1976; Schwartz & Myers, 1977*a*,*b*; Canton & Fraccon, 1985; Chung *et al*, 1986; Malla *et al*, 1990). The use of longer time periods does not appear to have diminished the likelihood of detecting elevated levels of stressors. Three of the five studies that used time periods of a month or less found evidence for elevated levels of stressors, whereas six of seven studies that used longer time periods found such evidence. This does not detract from the postulate that critical stressors may be most likely to occur within a few weeks of a worsening of symptoms. Indeed, results of analyses within studies by Day *et al* (1987) and Ventura *et al* (1989) support the finding by Brown & Birley (1968) that such a clustering of events in the few weeks immediately before change in symptoms is likely.

We should also note variation in the characteristics of the samples of schizophrenic patients. All of the studies in the first category used in-patients; five of the seven studies in the second were based on in-patients as opposed to out-patients; and only one of the studies in the third category was based entirely on in-patients. Could it be that the differences in the proportion of significant findings among the three groups are due to this difference in the composition of the samples, as opposed to the types of comparisons being made? Possibly, but it seems unlikely. Of the three studies in the second category with statistically significant results, two involved in-patients and one used out-patients. Furthermore, the one study in the third category that was based on an in-patient sample (Brown & Birley, 1968) did yield significant findings.

The studies we have reviewed extend over more than two decades (1967 to 1991) and were conducted in the UK, USA, and a number of other countries. Both these factors are likely to have influenced the diagnostic criteria used to define schizophrenia. For example, studies conducted in the USA before 1980 tended to use DSM–I and DSM–II criteria, which provided for a much looser definition of schizophrenia than DSM–III or ICD. The criterion of six months of deterioration in DSM–III is likely to have further restricted the diagnosis to the more severe cases, as compared with the use of ICD–9.

We have examined the publications in order to see if there was any relationship between the diagnostic criteria used and the findings with regard to stress and symptoms. The use of DSM–III, ICD or Kraepelinian criteria was regarded as stringent, while the use of DSM–I or DSM–II or failure to specify criteria was considered to imply relatively looser diagnosis. For studies reported in the first category, three used stringent criteria, while five used loose or unspecified diagnostic criteria. All reported negative results. For studies in the second category there are an equal number of positive and negative results for those using stringent and loose criteria. For comparison of stress and symptoms with schizophrenia, six of the eight studies used stringent diagnostic criteria and only one showed negative results, while one each showed positive and negative results among those studies using loose criteria. There

were also no differences in the results between studies using DSM-III and ICD criteria. These contrasts do not provide any substantial evidence for a difference in the strength of the relationship between stress and symptoms as a function of diagnostic criteria.

Some studies include only patients showing an initial onset of symptoms of schizophrenia, or, at least, the initial admission for such symptoms (e.g. Jacobs *et al*, 1974; Jacobs & Myers, 1976; Malzacher *et al*, 1981; Day *et al*, 1987). Other studies do not specify whether the patients were showing an initial or repeat onset and are, therefore, likely to have included both (Eisler & Polak, 1971; Beck & Worthen, 1972; Clancy *et al*, 1973; Leff *et al*, 1973; Schwartz & Myers, 1977*a*,*b*; Leff & Vaughn, 1980; Hardesty *et al*, 1985; Al Khani *et al*, 1986; Chung *et al*, 1986; Ventura *et al*, 1989; Malla *et al*, 1990). There is no significant difference in the proportion of positive results in these two groups. Of the three studies that contrasted stress levels between first onset and repeated onset, two (Lahniers & White, 1976; Skodol & Shrout, 1989) found evidence of higher levels of antecedent stress associated with initial onset, while the third (Canton & Fraccon, 1985) did not. In a possibly related contrast, Brown & Birley (1968) compared the number of life events reported to have happened before two types of onset of symptoms: change from normality or non-schizophrenic symptoms to schizophrenic symptoms, and change from mild to severe schizophrenic symptoms. There was no difference in the number of events reported as being antecedent to these types of changes. There is not, therefore, consistent evidence regarding the issue of whether initial onset of schizophrenic symptoms is typically associated with higher levels of life event stressors than repeat onsets.

One characteristic of samples that may be particularly important is whether or not patients are receiving neuroleptic medication. Almost all studies involve patients who are receiving medication. One exception is Leff *et al* (1973), who included a sample taking a placebo. The non-medication group did not show any evidence of a relationship between worsening of symptoms and antecedent stressor levels. These results are parallel to some non-significant trends reported by Birley & Brown (1970). Such findings suggest that patients without maintenance medication may be more likely to show worsening symptoms without major life events.

Conclusions

Our review suggests that there is a relationship between life events and changes in symptoms over time among individuals who are vulnerable to schizophrenia. The evidence for schizophrenic patients having higher levels of stress than the general population is weaker, and there is no evidence for schizophrenia being related to higher levels of life event stressors than other psychiatric disorders. These findings are consistent with models which suggest that the likelihood of developing symptoms of schizophrenia is a joint function of both vulnerability and stress encountered in dealing with the environment.

Acknowledgements, references, and authors' details are given at the end of paper II.

British Journal of Psychiatry (1993), **162**, 166–174

Stressful Life Events and Schizophrenia
II: Conceptual and Methodological Issues

ROSS M. G. NORMAN and ASHOK K. MALLA

Research on the relationship between stress and schizophrenia is fraught with conceptual and methodological problems. These problems include issues related to the nature and measurement of stress, the likelihood of reciprocal influences between stress and symptoms, and the adequate assessment of symptoms. Several recommendations are made regarding future research in this area. These include using multiple and broadly based measures of different types of stressors and symptoms, greater use of truly prospective research designs, and the evaluation of the effects of interventions specifically designed to reduce stress in patients who suffer from schizophrenia.