

## EDITORIAL

### Life events: effects and genesis<sup>1</sup>

It is more than 40 years since a burst of studies in the late 1960s started what has become a substantial corpus of work, establishing the role of life events in psychiatric disorders (Brown & Birley, 1968; Paykel *et al.* 1969). Findings depended on advances in methodology. First, came development of a life events questionnaire and a scaling of their stress magnitude (Holmes & Rahe, 1967); then, replacement by more reliable and valid interview methods and better ways of distinguishing major and minor events (Brown & Harris, 1978; Paykel, 1996).

At the start the work met entrenched opposing views – from one side that the real causes of psychiatric disorder were all constitutional, genetic and biological; from the other side that they lay in deeper, psychodynamic conflicts, originating in infancy and childhood. These polarizations in psychiatry have now greatly lessened. The general body of life event findings has become widely accepted. Recent stressful life events precede episodes of a variety of psychiatric disorders, particularly suicide attempts, and depression (Paykel & Cooper, 1992). The events are not very specific to disorders although there is some closer association with depression for events involving interpersonal loss, and those involving loss of self-esteem or humiliation. The effect is moderate in magnitude but varies with disorder – less in schizophrenia than depression, probably less in bipolar affective disorder than unipolar; within unipolar depression stronger in first episodes and milder disorders than in severe recurrent disorders. Effects are strongest near the onset of the disorder, and decay over time, with most of the effect occurring within 6 months to a year.

In this issue of *Psychological Medicine* we report six studies of life events. They use a variety of approaches to answer a number of questions.

Four papers, each using a different approach, involve depression, the disorder that has received most study. Rahman *et al.* (2003) extend to a rural community in Pakistan, questions regarding post-natal depression that have been examined in Western affluent populations. They find high prevalence of depression both 6 weeks before delivery and around 3 months post-natally, and strong associations with severe events and difficulties in the previous year. These findings are similar to those obtained in the Western world (Paykel *et al.* 1980; O'Hara, 1986). In this much more deprived population the events reported by women were also mainly similar, with marital and family problems looming large, although events involving economic hardships such as loss of job by the breadwinner and financial difficulties were also prominent, as might be expected.

This kind of life event case–control study has a long history and continues to appear. In another recent paper Brilman & Ormel (2001) used a nested case–control design in a large community survey of elderly people, and found a strong effect for severe life events on depressive episodes, particularly first episodes. Rubenowitz *et al.* (2001) used a case–control approach with informant interview to show effects of familial problems and family discord on suicide. Maciejewski *et al.* (2001) in a community survey found women more likely than men to experience an episode of depression after a major event. However, such studies are now mainly replicatory.

Farmer & McGuffin (2003), a distinguished husband and wife pair who have made notable contributions to psychiatric genetics, adopt a sib-pair approach to study issues arising directly from the work of George Brown on the qualities of events which are important. Siblings share some of both the social background and genetic load of the probands. Farmer & McGuffin find depressives more likely to have experienced a severe threatening event, loss event or humiliation

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event, than their siblings or general population controls. Depressed men were more often exposed to humiliation events than depressed women. Could this have been a consequence of males tending to compete in work-related hierarchies? The authors also report some evidence that exposure to non-severe events protect, perhaps by enhancing coping. Here replication is needed: the previous studies that have looked at non-severe events have found little effect, or a weak stress-additive effect.

In previous sib-pair work using this sample (Farmer *et al.* 2001 *a*) sensation-seeking questionnaire scores showed a familial element and were associated with more events of low threat, but were not associated with the higher threat events related to depression, and showed an inverse association with depression itself. In another analysis dysfunctional attitudes were only very weakly familial and were mainly determined by low mood (Farmer *et al.* 2001 *b*). In another sib-pair sample (Rijsdijk *et al.* 2001) this group found moderate familiarity for network events, less for personal events. Adverse life events were associated with depression and anxiety.

Kessing *et al.* (2003) use a different approach, record linkage, to examine major events and first hospital admission for depression. The advantage is reliable event data not affected by patient or interviewer distortions. The disadvantage is that only a few, very major events, are recorded this way, and hospital admission is not the same as onset of disorder, and may have its own separate social influences. They find effects of divorce, recent unemployment, and suicide of first-degree relative, but not other deaths. The effect is constant over the adult lifespan.

These three studies of depression represent a tidying up of remaining questions and replications by different methods. Other life event approaches include more general epidemiological studies, used in recent years to study various social stress risk factors. Thus, aircraft noise was found by Haines *et al.* (2001) in a sample of school children to affect reading comprehension and noise annoyance, but not psychiatric symptoms. Absence of social support was found by Brugha *et al.* (2003) to be associated with type of adult neurotic symptoms, particularly depression. Impact of work related factors has been found to be greater in males than females and in working class rather than higher social class subjects (Matthews *et al.* 2001). Impact of job strain has also been reported on coronary heart disease (Sacker *et al.* 2001). Another approach is the prospective study of the specific event – a very good way of studying modifying factors. This approach is inherent in much of the modern literature on post traumatic stress disorder, and the kind of events which precede it (Emmelkamp *et al.* 2002).

Hatcher & House (2003) tackle a newer area where the degree of psychological aetiology is still argued: chronic fatigue syndrome. They use the Bedford College Interview and a classical retrospective case-control design. Their subjects with chronic fatigue syndrome were more likely than general population controls to have experienced severe events and difficulties in the 3 months before onset, with a high odds ratio, and a smaller effect over 1 year. These authors also report a new class of event, a dilemma, which strongly distinguishes subjects and controls. The idea derives from concepts of conflict in conversion disorder. It needs more study in other disorders, to determine if there is specificity.

Kendler *et al.* (2003 *a*) report in this issue a further study in an important series exploring a rich vein – what causes a life event? Clearly life events are not always simply external random occurrences: we all, by earlier life decisions, social-setting and lifestyle, influence the life events from which we suffer.

One element in this is genetic (Plomin *et al.* 1990). Kendler and colleagues have made productive use of twin studies. They used the large Virginia twin registry, and first obtained postal questionnaire reports of occurrence of 44 life events in the past year (Kendler *et al.* 1993). Correlations were a little higher in monozygotic twins than dizygotic. Genetic and common environmental elements each accounted for about 20% of the variance, with the former predominant in 'network' events affecting individuals in the respondent's social networks, and the latter higher for 'personal' events directly affecting the respondent. In later waves, information was collected by interview. Genetic elements affected liability to develop depression after life events (Kendler *et al.* 1995). Genetic liability to major depression increased the risk of being exposed to life events, mainly personal ones, outside the depressive episode (Kendler & Karkowski-Shuman, 1997). Alcoholism increased risk of

being robbed and having trouble with the law. About one-third of the relationship between life events and depression appeared to be non-causal, due to self-selection into high risk environments (Kendler *et al.* 1999*a*). In a further paper (Kendler *et al.* 1999*b*), no evidence was found for genetic effects on independent events of personal or network classes, but the latter showed considerable effects of familial environment. Dependent events showed genetic effects. Recently this group have also found genetic elements in social support (Agrawal *et al.* 2002). They have also used discordant twin pairs to study recent life events and early stress factors unique to the individual and not reflecting genetic factors or family of origin effects (Kendler & Gardner, 2001).

In the current paper (Kendler *et al.* 2003*a*), they examine the association between the personality traits of neuroticism and both stressful life events and the quality of interpersonal relationships. They had previously confirmed the heritability of neuroticism (Kendler *et al.* 2003*b*). They now report a complex analysis using earlier reports by twins of neuroticism, and later reported life events and interpersonal dimensions from a social interaction measure. They find neuroticism to predict occurrence of most life events and all interpersonal dimensions. This is not due to reporting bias as it also applies to neuroticism in the subjects as reported by the co-twin.

In the sixth paper in this issue, which returns to depression, Patton *et al.* (2003) use a different approach to what is cause and what is consequence by studying the occurrence of life events and of depression over two waves in an epidemiological community study of adolescents. They find previous depression and anxiety to predict later events, and events in turn to predict later depression, even without previous symptoms.

In earlier work on related issues, Champion *et al.* (1995) found that children who had shown emotional or behavioural disturbance aged 10, when studied in their late 20s had markedly higher rates in the 5 years before the follow-up interview of highly threatening events and difficulties, both dependent and independent. Van Os & Jones (1999), using a longitudinal birth cohort, found that stressful life events in midlife were predicted by high neuroticism in childhood. This measure also predicted stronger effects of life events on disorder.

An emerging area of major importance concerns mechanisms – how do life events induce disorder? In a recent unusual study Myin-Germeys *et al.* (2003) found evidence that major life events produced their effects on patients with remitted psychotic illness by increasing emotional reactivity to minor daily stresses. Does this indicate a biological, brain mediated effect? In the long run, the effects of stress on psychiatric symptoms and disorder must be through the brain, and brain–social stress interactions are ripe for study, in animals and humans. Interactions with early disease processes, personal characteristics such as gender and personality, equally require further study.

We have achieved the recognition that causative sequences are complex, and should not be viewed in simple black or white terms of environment or genes, social stress or brain and other biology. Both are intertwined. There will be more of this research in the future as the causative chains, the interactions between their elements and the mechanisms are more fully elucidated.

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