

Life events, stress and depression: a review of recent findings

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Objective: To review recent empirical prospective studies on the relation between life event stressors and depression.

Method: A systematic literature search focusing on predictive studies was carried out from 1980 to early 2001 using *Medline*, *Embase* and *PsychInfo*.

Results: The empirical findings for the most part support clinical impressions of the relation of stressors to depression but at the same time provide some clearer understanding in relation to differences of stressor impact on depression type and on index episode, relapse or recurrence. Twin studies now provide the strongest evidence of the relative magnitude of effect of environmental stressors and genetic factors: the former explains at least as much of the variance in depression as our genes.

Conclusions: Continuing research into life events and depression have been fruitful especially those studies assessing the effect of stressors in combination with other aetiological variables such as genetic factors.

Key words: depression, genetics, life events, stress.

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A wealth of published evidence shows that life event stressors are associated with the onset of depressive episodes and that there is a dose–response relationships [1]. In reviewing the evidence, it is, however, important to distinguish the effects of antecedent and intercurrent acute life events and chronic difficulties and to also distinguish their impact on the severity, type and outcome of the index episode, and the risk of relapse and later recurrence. Recent findings assist in refining our understanding of the relationship in this regard. It is also important to consider the effect of other variables which can moderate or confound the relationship or indeed interact in other ways. In this latter regard recent genetic studies are important. This review focuses largely on prospective studies published in the last 20 years and identified through systematic literature searches being *Medline*, *PsychInfo* and *EmBase*. The search terms used

were stress, life event stress, stressors and, depression, depressive disorders and affective disorders. No attempt was made to identify unpublished studies as such a task was too formidable. A meta-analysis was not considered as the studies embrace a large diversity of method and effect size is not readily assessable as it is for example in randomized controlled treatment trials.

Life events and course of depression

Severity and duration of index episode

Stressors are associated with greater initial severity of depressive symptoms both in adult patients [2] in ‘non-patient’ community samples [3] and in adolescent depression [4–6]. Stressors are, however, associated with fewer vegetative features both in depressed patient samples [7,8] and in the community [8]. Stressor severity also predicts depression severity in other patient groups such as in schizophrenia [9] and in the elderly post-CVA [10].

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In relation to the duration of the index episode in depressed patient samples, antecedent stressors in two studies are reported to impede recovery [1,11], but most other studies report there is a more rapid recovery, including in psychotic depression [12], endogenous depression [13,14], and depression in a community setting [3]. These 'inconsistent' findings may reflect, firstly, sample differences both in the type of stressors and of disorder; in the community, for example, more acute 'reactive' episodes are likely whereas in some patient groups, chronic stressors and more enduring depression seem likely. Secondly, the disparity may reflect the failure in many studies to adequately distinguish acute antecedent stressors from chronic (ongoing/intercurrent) stressors. The latter are certainly known to delay the resolution of index episodes [15,16].

The immediate and long-term impact of the same stressor may also differ. For instance, Vietnam veterans exposed to heavy combat were more likely to have emotional disorders in immediate post-war years than were veteran controls with less combat stress, but by mid-life they appeared more resilient than the controls [17]. This suggests the possibility either that stressors which cause early psychological impairment can over the long-term enhance psychological resilience, or that those combatants identified with more (expressed) stress symptoms in response to any combat stressor are in fact more emotionally resilient individuals in the longer term.

Relapse and recurrence

It is also important to distinguish antecedent stressors from intercurrent or concurrent stressors. Findings from studies of the former are methodologically stronger because they are clearly predictive. Antecedent stressors (as well as intercurrent) predicted poorer outcome in treated depression at 3 months [18], at 4 months [11] and, 6 months in the elderly following a CVA [19], while two or more acute events or a chronic difficulty predicted poor depression outcome over 12 months in the community [20]. Intercurrent stressors not unexpectedly correlated with poorer prognosis over both 6 months [21] and 11 years in adults [22] and over 6 months [23] and 4 years [24] in adolescents and young adults.

The importance of distinguishing acute from chronic stressors and distinguishing index episode duration from relapse or recurrence is highlighted in findings, from the following studies. Firstly, in endogenous depressed patients, antecedent acute events predicted good initial treatment response and low relapse rates while chronic (ongoing) difficulties were associated with more frequent relapse [14]. Secondly, while patients with 'environmentally

sensitive' episodes of depression had a longer initial episode, they had fewer episodes overall than did patients with an 'environmentally unrelated' disorder [25]. Finally, chronic stressors (namely medical illness and family conflict) were found to adversely affect depressive disorder both one and 4 years later, while acute life events did not [26].

In relation to recurrence of depression, there are some important issues. Recurrences may themselves be precipitated by (dependent) life stressors caused by an earlier episode [27]. Furthermore it appears the number of recurrent episodes is important, since the severity of stressors generally required to precipitate subsequent episodes of disorder increasingly diminishes both in adults [28–30], and adolescents [31]. It has been postulated that kindling or sensitization to stressors may indeed become encoded at some level of genomic expression [29,30]. Finally, this kindling effect seems most marked in subjects with low genetic risk and less so in those with high genetic risk [32].

In summary, acute stressors seem to be associated with more depressive symptoms but with a better immediate outcome. The longer term prognosis (relapse, recurrence) may be adversely affected by stressors causing a kindling effect and/or some acute stressors becoming chronic. Finally, antecedent chronic stressors and intercurrent stressors (both acute and chronic) are associated with poorer prognosis of the index episode, and with more frequent relapse or later recurrence.

Stressful events and type of depressive disorder

Various studies have assessed stressful events in relation to depression type: these include postnatal depression, 'endogenous' or 'neurotic' depression, major depression or non-major depression, unipolar or bipolar and, depressive disorders with and without a strong family history.

Postnatal disorder

While post-partum blues are predicted by life events [33], strangely perhaps there is no good evidence that they have any substantial causal role in more serious postnatal depression. Life events predicted neither postnatal psychoses [34–36], nor postnatal depression [37–39], although in the latter study a concurrent association was found. In another study, stressors predicted depression relapse but only in previously depressed postnatal women [36]. Paradoxically perhaps, one study has reported antenatal depression was more strongly stressor related than postnatal depression [40].

Syndromal type

Unipolar depression

In one study of depressed outpatients there was a similar clinical syndrome in three patient subgroups: those either with a severe 'interpersonal' stressor, with 'other' stressors and those without a stressor [13]. Other studies have, however, found syndromal differences: less guilt and fewer vegetative symptoms were found both in depressed patients [7] and in depressives in the community who had experienced stressors [41]. Life events nonetheless can precipitate both 'neurotic' and 'endogenous' episodes [41,42], although the association appears stronger in 'non-endogenous' depression [42].

Within an endogenous depressive group, stressors were associated with both psychotic and non-psychotic symptoms [43]. Similarly, in non-melancholic major depression where, latent class analysis identified four depressive clinical sub groups: stressors did not distinguish these groups [44]. Stressors are, however, more often associated with cognitive, affective and suicidal symptoms than with somatic symptoms [45]. Finally, 'hassles' were found to be more common in dysthymia than in major depression, and they tended to diminish with effective treatment [46], suggesting indeed they were the consequence of the chronic mood disturbance.

Bipolar disorder

It appears stressors can trigger both hypomania and depression [47] although unipolar major depressives had more antecedent stressors than did bipolar subjects [14]. In bipolar disorder, family stressors in particular seem more common [47] as are 'illness independent' stressors which cause a 'disruption in sleep-wake cycle' [48].

Anxiety versus depression

Stressful events in the community predict both depression and general anxiety [3,49,50]. In relation to the severity of stressors, however, depression was precipitated only by 'severe' events, whereas anxiety was provoked by events of a wider range of severity [51]. In an elderly sample with comorbid anxiety and depressive disorders, while adverse life events were found to be associated with anxiety syndromes, this relationship seemed largely mediated by their relation to the depressive disorder [52].

Different types of stressor have been assessed in relation to either depression or anxiety, most commonly in 'non-clinical' samples. Recent stressful life events predicted anxiety while daily hassles predicted depression

in university students [53]. In women in the community, 'loss' events were associated with depressive disorder and 'danger' with anxiety disorder [54,55], while events combining 'loss' and 'danger' caused both depression and anxiety symptoms [54]. In the same community study, chronic childhood stressors ('neglect' and 'abuse' in childhood) predisposed to both adult depression and anxiety [56] while chronic adult adversity (e.g. widowhood) was associated with depression alone [57].

Type and quality of stressors

Chronicity or duration of stressors

Both acute and chronic stress were associated with depression in adults and their effects were additive [51,57]. Chronic stressors, however, have a greater impact on depression than do acute events [58] and not surprisingly, are found to be associated with depression over a longer 'at risk' period [50,59]. Similarly, the accumulation of total stressors over 2 years is a stronger predictor of relapse than other stressor assessments over shorter time frames [18].

Timing of stressors and onset of disorder

Recency and dissipation of effect

Most studies show the effect of stressors (especially acute stressors) dissipates with the passage of time. This is reflected in findings that 'most recent' stressors have greatest impact [60]. A 'dissipation' effect is also found with chronic stressors. Recent chronic difficulties for instance predicted both depression and anxiety disorders [51] while more distant difficulties did not.

For acute life events, while recent ('precipitating') events and more distant ('incubating') events were both statistically significant in provoking depression (both endogenous and neurotic syndromes) [60], 'incubation' events had lesser impact than 'precipitation' events and were significant only in women [60]. Particularly important indeed are acute events found in the month prior to onset [41,50]; however, up to a 7-week risk period prior to onset was found in another study [61]. Chronic difficulties on the other hand, however, can exert an effect over a longer period being 6 months in one study [50] or up to 1 year in another [62].

Childhood and adult stressors

The distinction between *childhood and adult* stressors is also important. In relation to earlier childhood experiences the evidence is somewhat inconsistent. Childhood

sexual and physical abuse were both independently associated with adult depression in women [54,55,63–65], while childhood stressors were found to ‘sensitize’ women to stressor induced depression in adult life in another study [66]. Similarly in elderly depressives, both recent events and significant events earlier in life separately predicted depression [67]. Finally, two review articles on early childhood ‘loss’ experiences [68,69], concluded that parental divorce predicted adult depression but parental death in childhood did not. Thus it seems clear that significant ongoing childhood stressors are indeed predictors of much later (adult) depression.

Domain of life stress

A wide range of event types can provoke depression. Marital, health, or housing stressors were significant in Pakistani depressed women in the United Kingdom [70], while in depressed mothers, spousal abuse, earlier child abuse and other stressors were significant [64]. In unipolar depressed women, ‘interpersonal stress’ events and ‘dependent’ events were common [27], while death of a relative, assault, divorce or serious marital conflict were found to be significant in female twins [71]. In men and women, both work and family stress were associated with depressive disorders [72], while 4-year outcome in unipolar depression was predicted by pre-existing medical illness and family conflicts [26]. ‘Interpersonal stressors’ were associated with better outcome in an index depressive episode, while two ‘achievement’ events were associated with worse outcome [73]. These differences may be due to chronicity of stressors in the latter instance. Relationship stressors thus seem to emerge generally as prominent in causing adult depression, particularly in women.

Quality of stressors

‘Personally relevant’ events and those linked to ‘self-worth’ predicted 3-month outcome in unipolar depression adults [74]; ‘fateful’ and ‘disruptive’ events are also significant [75] and, events involving ‘humiliation’, ‘entrapment in a difficult relationship’ or bereavement were similarly significant in women [76,77]. Finally, some life events can also trigger remission in depressive disorders; these have been termed ‘neutralizing events’ [78] or ‘fresh start events’ [79].

In children, ‘loss’ events were associated with depression, while conflict events [80] and personally stressful events [81] predicted conduct problems. In adolescents, inconsistent parenting [82], interpersonal conflicts and physical illness [83], and family conflicts [6]

all predicted depression. In suicidal adolescents [83], separations, poor parental supports, or disciplinary conflicts further contributed to comorbid alcohol abuse.

In young people not only do their own personal stressors affect depression, but stressors in their parents have a significant impact. Maternal ‘stress’ [5,84], parental depression [82] and maternal stressful events [82,84] predicted adolescent depression and behaviour problems in children [81].

Possible moderating variables

Personality, life events and depressive states

‘Personality’ variables are frequently a covariate in the relation between life event stress and depressive states: they may be an independent risk factor for depressive disorder, they may moderate the effects of life stress on depression or, finally, personality may actually confound the association by contributing separately both to risk of life events and to depression (there being no true causal link between them).

Most ‘personality’ studies are of ‘non-clinical’ populations, such as university students. In some studies, life stressors and personality variables had independent effects (with no interaction between them); these include studies of negative cognitions [85,86], ‘poor ego’ [87], ‘poor mastery’ [88] and sociotropy/autonomy [73].

Others studies have shown some ‘interaction’ or synergy between life events and personality including such variables as dysfunctional attitudes [89], depression-prone personality [90], sense of humour [91], self esteem [92], self complexity [93], inhibition of anger [94], attributional style [95], sociotropy autonomy [96] and, perceived competence [97].

Specific types of stressor have been assessed in conjunction with specific personality traits; most commonly used is the personality trait of ‘self-criticism’. In ‘independent subjects’, only ‘interpersonal’ events predicted depression, while in ‘self-critical’ subjects, both ‘interpersonal’ and ‘achievement-oriented’ events contributed to depression [98] and the latter, also to relapse in depression [99]. ‘Self criticism’ in females also increased the impact of stressors generally while in males ‘dependency’, increased depression-risk [100]. Finally, sociotropy/autonomy interacted with interpersonal stressors on depression risk [96].

‘Masculine–feminine’ identity has also been studied in non-clinical (university student) groups to determine whether ‘feminine personality’ traits contribute to women’s greater risk of depression. Female gender stereotype and life events independently contributed to depressive risk (with the latter having the greater effect) [101], while in

two other studies, a female gender stereotype potentiated the effect of life events in causing depression [102,103].

Thus, while personality may confound the association between stressors and depression, it is at least an independent causal factor for depression, while other studies reveal some additional interaction effect.

Social supports, life events and depression

Most studies show no buffering or moderating effect for social supports in the stress/depression relationship. Independent causal effects are found in many different samples, being depressed adults [104,105], older depressed women [106], community samples [54,57,107], bereaved subjects [108], the physically disabled [88], university students [109], professional employees [73] and female twins [110]. Support for the buffering hypothesis is found in few studies; most of these studies (like studies of personality) are in non-clinical samples (university students) and tend to assess depressive symptoms rather than ‘disorder’ [111–113].

Social supports have also been studied in adolescents. Positive ‘social circumstances’ buffered the effect of life stressors on depression [114], ‘peer groups’ acted as a buffer for boys, while ‘family relationships’ were a buffer for girls [115], however, stressors and ‘social resources’ were independent in predicting depression in adolescent mothers [116]. Similarly, perceived parental warmth in childhood, familial stressors and childhood abuse were independently associated with depression in adult women; parental warmth, however, also further moderated the effects of childhood abuse on depression risk [117]. Finally life events can also effect social support directly: some life events are associated with decreased seeking of social support, while others have no such effect [118].

Genes, gender, life events and depression

Gender, life events and depression

Stressors may both be more common in adult women than in men [41] and there may also be a stronger relationship between stressors and depression in adult women [41,60,87,119,120], in adolescent girls [121] and in elderly females [122–124]. Female vulnerability to stressors was, however, not found in a twin study where men and women had similar ‘event sensitivity’, although the sexes differed in their sensitivity to specific events [125]; these were divorce/separation and work in men and interpersonal stressors in women. The assumption that the excessive risk of depression in women is largely due to environmental stressors is, however, further supported firstly by findings from a twin study

showing there was no sex difference in genetic risk [126] and secondly, in women of ‘menopausal’ age, where age-related life stressors (not the menopause itself) predicted later depression [127,128].

Family history

Family history of depression has no particular influence on the relationship of life stress to depressive disorder. Firstly, there is no obvious inverse relation between familial (genetic) depression and stressor-induced depression as might be suggested by the constructs of reactive and endogenous depression [129–132]. Secondly, there appears to be no ‘breeding true’ of stress-related depressive disorder within particular families [131]; first-degree relatives of subjects with stress induced depression are not significantly more likely to experience depression due to life events than first degree relatives of depressed patients with a stressor induced episode [131]. There is, however, a reasonable ‘familiality’ in siblings, life event experiences, correlations ranging from 0.1 for ‘personal events’ to 0.37 for ‘network events’ [133].

In the case of bipolar disorder however, life stressors were associated with later onset and positive family history with earlier onset and, there was an inverse association between life stressors and positive family history in this sample [134].

Twin studies

Twin studies have provided the strongest evidence of the relative magnitude of effect of environmental stressors and genetic factors on depression risk. In one study of 2164 female twins, life stressors explained more of the variance in depression [0.39] than either genetic factors [0.33], past history of depression [0.30] or neuroticism [0.25] [135]. However, one-third of the total variance between life events and depression was ‘non-causal’ and was explained by individuals at high risk of depression selecting into high ‘stress risk’ environments [136]. Certain life events were genetically determined since some life events correlated strongly within twin pairs, especially in monozygotic pairs. Furthermore, both genetic factors and childhood familial environment each separately contributed about 20% of the variance in life stressors experienced [137] and both also influenced social support and risk of depression [110].

The best-fitting causal model for depression suggested that stressful life events and genetic factors interact [71]. In the lowest genetic risk group (monozygotic discordant for depression) risk of depression over a 1-month period was 0.5% in those unexposed to a stressor and 6.2% in

those exposed, while in the highest genetic risk group (monozygotic twins concordant for depression) the equivalent risks were 1.1% and 14.6%, respectively. Linear regressions indicated significant genotype-environment interaction in predicting onset of major depression in this sample [71]. In other twin studies, a common genetic liability to both experiencing life stressors and depression has also been reported in adult male twins [138], in adult twins of both sexes [139] and in adolescent twins [121,140,141].

Finally, genetic factors may influence other 'stressor related' variables: these include firstly the sensitivity of individuals to the effect of a stressor [71], and secondly the reporting of stressors, particularly those over which the subject has some control [138,142]. The latter findings are consistent with those showing that the genetic liability for depression (rather than mood disturbance itself) accounted for an increased risk of 'dependent' events including assault, marital problems, divorce, job loss, major financial problems and other interpersonal problems [71].

In adult twin studies the nature of environmental vulnerability has been studied: it appears to be the 'non-shared' (adult) environmental stressors which contribute most to depression, whereas the 'shared' childhood (family) environment in twins does not [143-145]. One innovative study of adoption in twins found 'heritability' of depressive symptoms was only 16%; family rearing made a significant contribution but unique life stressors made the greatest contribution [146]. Similarly, in a twin study of children and adolescents, the shared (family) environment explained most symptoms in younger children where in older adolescents genetic factors accounted for more symptoms [141].

Vulnerability to the effect of stressors is in part genetically-determined. This has been demonstrated firstly in twin studies [71,138-141]. Secondly, first-degree relatives of subjects with depression have been shown to have a personality type which is vulnerable to stress; it is characterized by autonomic lability and rigidity [147]. Thirdly, second generation female offspring of parents exposed to a catastrophic stress (the holocaust) were found to have greater depression following their experience of the same stressful event (diagnosis of breast cancer) than women whose parents did not experience the holocaust [148]. Sensitivity to stressors is influenced by genetic factors and is transmitted across generations.

Discussion

This review process has some limitations. Firstly, unpublished studies were not identified. This may bias the

'data' toward studies reporting positive findings. Despite there being an increasing trend toward meta-analyses, these type of aetiology studies do not lend well to such an approach. The studies reviewed, however, were identified in a systematic fashion using a variety of key words and three different literature searches.

There are some methodological factors in life stress studies, which may contribute to at least a partially confounded relationship between life stress and depression [149]. If, however, appropriate life event assessments and a prospective design are used, this problem is largely excluded: this review is of prospective studies. The recent studies reviewed demonstrate a consistent significant relation between stressors and depression. Acute stressors are in all probability associated with a briefer illness episode with an 'at risk period' of a month or so; chronic stressors (lasting 6 months or more) have a much longer at risk period, cause longer episodes and contribute to a greater relapse/recurrence rate. None of this is too surprising from a clinician's perspective.

Both personality and social support are found to be separate risk factors for depression although there is some evidence personality has an additional moderating effect on the relationship between stressors and depression.

Both contemporary (adult) and earlier (childhood) stressors are risk factors. There is little support for the notion, however, that childhood stressor exposure sensitizes subjects to later stressor-induced depression.

In relation to 'sensitization', however, there is good evidence that a prior depressive episode sensitizes individuals to subsequent stress induced disorder; lower levels of stress can trigger subsequent episodes. The notion of kindling has been proposed to explain this phenomenon. This sensitization/kindling is weaker or absent in subjects with a high genetic loading for depression.

Finally, twin studies have made the most significant contribution to understanding the relative impact of genetic factors and life stressors on depression. In normal populations, the impact of stressors on depression is at least as strong as genetic effects; each contribute to over 30% of the variance. In clinical samples, the genetic effect may, however, be more substantial. In terms of childhood and adult stressors in twins, the latter is a substantial causal variable while stressors arising in the (shared) familial environment is not. In considering the 'aetiology' of stressor exposure, twin studies show that both a genetic effect and the shared family environment in childhood each contribute to 20% of the variance in adult life event stress. Finally, the most parsimonious model for depression shows an interaction between genetic risk and adult life stressors in causing depression.

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