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STRESS AND DEPRESSION

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■ **Abstract** Improved methods of assessment and research design have established a robust and causal association between stressful life events and major depressive episodes. The chapter reviews these developments briefly and attempts to identify gaps in the field and new directions in recent research. There are notable shortcomings in several important topics: measurement and evaluation of chronic stress and depression; exploration of potentially different processes of stress and depression associated with first-onset versus recurrent episodes; possible gender differences in exposure and reactivity to stressors; testing kindling/sensitization processes; longitudinal tests of diathesis-stress models; and understanding biological stress processes associated with naturally occurring stress and depressive outcomes. There is growing interest in moving away from unidirectional models of the stress-depression association, toward recognition of the effects of contexts and personal characteristics on the occurrence of stressors, and on the likelihood of progressive and dynamic relationships between stress and depression over time—including effects of childhood and lifetime stress exposure on later reactivity to stress.

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INTRODUCTION

Several excellent and widely cited reviews have been written on the topic of stress and depression in the past 15 years (e.g., Kessler 1997, Mazure 1998, Monroe & Hadjiyannakis 2002, Paykel 2003, Tenant 2002). Therefore, one challenge of the current chapter is to provide a useful brief summary of the state of the field, yet include coverage that is forward-looking enough to avoid duplication of prior reviews. Accordingly, particular attention is devoted to emerging topics in this field, or to highlighting interesting topics with significant conceptual or empirical gaps—admittedly subjective decisions. A second challenge is that this is a huge field, with major works emerging not only in clinical psychology, but also in sociology, psychiatry, and public health/epidemiology. Hundreds of articles have been published in just the past few years. Thus, it is necessary to be selective, with no pretense of comprehensive and exhaustive reporting. Coverage focuses on relatively more recent work, mostly based on longitudinal studies, addressing adult unipolar depressive disorders rather than symptom outcomes. (There are some exceptions if relevant work is distinctive, informative, or illustrative of key points.) The chapter starts with an affirmation of the empirical link between stress and depression, and the methodological issues in stress measurement, followed by sections that address several questions in the stress-depression relationship: what kind of stress, what kind of depression, and what kind of relationship?

OVERALL EVIDENCE OF A CAUSAL RELATIONSHIP AND METHODOLOGICAL ISSUES

A substantial body of research using state-of-the-art interview measures of episodic life events has found higher levels of significant stressors prior to the onset of major depressive episodes in patients compared to controls, and in community samples (e.g., reviewed in Brown & Harris 1989, Mazure 1998). Mazure summarized findings—many based on Brown & Harris's (1978) Life Events and Difficulties Schedule—noting that stressors were 2.5 times more likely in depressed patients compared to controls, and that in community samples, 80% of depressed cases were preceded by major life events. Note that the great majority of these studies were based on female samples. Significant associations between prior stressors

and depression have been confirmed by the most stringent test—"independent" or fateful events that could not have been due to the individual's depression or other characteristics (e.g., Shrout et al. 1989, summarized in Mazure 1998). Other contributions have included genetic studies of twin pairs (e.g., Kendler et al. 1999), and "natural" experiments that occur when exposure to the event is random and independent of depressive outcomes—such as widowhood, and exposure to natural disaster (reviewed in Kessler 1997). Overall, therefore, the recent evidence based on sound methods of stress assessment and novel designs strongly suggests that most episodes of major depression are preceded by stressful life events (although most people do not become depressed even if they experience a negative life event).

Methodological Issues in Stress Assessment

There have been two major challenges to stress measurement over the years: making certain that the stress is not confounded with the outcome, depression, that it purports to predict, and ensuring that the "stressfulness" of an event can be understood from the point of view of the individual's personal circumstances. Life event checklists generally have been found to be limited on both accounts (see Kessler 1997 for discussion of the history of life event checklist usage and relevant issues). Endorsement of checklist items and their severity ratings might reflect subjective, idiosyncratic meanings and judgments that are affected and possibly biased by the emotional state of the person, and each item selected could have personal meanings that would vary from person to person (e.g., death of a close family member might have enormously different meanings depending on the circumstances of a person's life). Although improved methods of checklist assessment that do not require subjective ratings have been developed, checklists continue to have the drawback of including only limited numbers of events, and each item may reflect highly personal meanings that preclude full understanding of the individual's objective circumstances.

Interview methods have been developed to address both the bias and personal meaning issues, and are generally regarded as the standards of the field. George Brown and colleagues (e.g., Brown & Harris 1978) developed the method of contextual assessment of stressor severity, whereby event occurrences are identified systematically and the circumstances surrounding the event are probed. Such contextual information is then used as a basis for rating the "objective" threat of the stressor in terms of how a typical person under identical circumstances would experience the event, but without accessing information about how the individual emotionally reacted to the event. The Life Events and Difficulties Schedule (Brown & Harris 1989) also elicits specific information about the timing of the event onset and its duration, permitting definitions of both acute events and "ongoing difficulties," and the extent to which the event was likely caused at least in part by the respondent or was independent of the individual (fateful). Objective raters later score events and difficulties; a "dictionary" of events and ratings has been accumulated to guide ratings of severity depending on individual context. Interview procedures using semistructured contextual methods have also been developed by

Paykel (1997), Dohrenwend (Dohrenwend et al. 1993), and Hammen (Hammen et al. 1985, Hammen 1991), among others.

Research comparing the interview methods (and objective measures of stress severity) and checklist methods has generally confirmed that the former are more effective in predicting outcomes, more accurate in terms of recall and precise dating of event occurrence, and less subject to the bias conferred by mood and current cognitive vulnerabilities (e.g., McQuaid et al. 2000, Simons et al. 1993). Despite their advantages, however, the contextual-based interview methods have certain drawbacks, including requirements for interviewer training and labor-intensive objective threat-rating procedures. Also, it has been noted that "context" information that is elicited and folded into the threat ratings may itself consist of risk factors that account for the association between the purported event and depression (Kessler 1997, Mazure 1998).

THE RELATIONSHIP BETWEEN STRESS AND DEPRESSION: WHAT KIND OF STRESS?

The vast majority of research supporting a relationship between stress and depressive episodes has been based on episodic stressors (discrete events that have a beginning and ending) that have negative or undesirable content. The metric for analyzing stress-depression associations has variously been counts of events aggregated across content and time, total ratings of "stressfulness" across events, or most commonly, presence/absence of at least one stressor of moderate to severe impact (e.g., Brown & Harris 1978). There is some evidence of a generally linear association between severity and number of negative events and probability of depression onset (Kendler et al. 1998).

Although studies tend to differ in the time frame of event assessment preceding depressive onsets, most studies typically include three or six months. Brown & Harris (1978), in their classic study of depression in women, found that most severe events rapidly lead to depression (especially in the first three weeks after a negative event), and Kendler et al. (1998) found that the great majority of life events associated with major depression onset occurred within the first month after the event.

Stressor Content

Are all stressors equally likely to precipitate depressive reactions? Does content matter? Apart from agreement that depression may follow undesirable events, and setting aside the truism that *any* event may have personal meaning and significance for an individual, researchers have explored whether some classes of events are especially likely to provoke depressive reactions. The most venerable and extensive line of research has focused on the unique significance for depression of interpersonal "loss," which may include bereavement, separations, endings—or threats of separation. Paykel & Cooper (1992, also Paykel 2003) reviewed studies showing

that such "exit" events often precede depression, and may be more common in depressed samples than in other forms of psychopathology. Tennant (2002, see also Kendler et al. 1995) also suggested that relationship stressors—many of which are loss or threatened-loss events—are common in depression, perhaps especially for women. The concept of loss sometimes has been expanded beyond interpersonal exit events to include loss of self-esteem, role loss, or loss of cherished ideas (e.g., Brown et al. 1995, Finlay-Jones & Brown 1981).

"Dependent" events to which the person has contributed (in contrast to fateful, independent events) include most interpersonal events as well as many that define sources of self-esteem such as work and finances; dependent events are more predictive of depression onsets than are independent events (Kendler et al. 1999). Although it seems that interpersonal loss experiences are especially predictive of depression, the specificity of such experiences for depression and the mechanisms involved remain questions for further study.

Content by Personality/Cognitive Match

A refinement in the prediction of depressive reactions to stressors concerns the hypothesis that depression is most likely to occur when there is a match or congruence between the individual's personality styles or schemas and the occurrence of a stressor whose content is relevant to the personality style. The hypothesis arose from similar views of Beck (1983) and Blatt (1974) that individuals may have depression vulnerabilities that are specific to critical sources of self-worth, noting the centrality of values attached to sociality or to achievement. The cognitive and psychodynamic constructs of sociotropy and dependence, or autonomy and self-criticism, have both similar and distinct features, but the models agree that individual differences in the strength of these personality or schema features determine how stressors will be interpreted, and stress appraisals that represent threats or depletion in the core areas of self-worth will lead to depressive reactions. Thus, a person with high sociotropic values would be more likely than someone without such beliefs to interpret an interpersonal loss experience as highly significant and reflecting personal shortcomings, potentially triggering depression.

These models have stimulated a fair amount of research, mostly supportive of the congruency model (e.g., reviewed in Nietzel & Harris 1990), and some controversy. Coyne & Whiffen (1995) wrote a lengthy conceptual and methodological critique, accurately depicting some of the limits of the early efforts to test the model. However, Zuroff et al. (2004) recently responded in depth to the criticisms, noting further developments in the field that serve to make a strong case for viewing the personality or schema styles as valid candidates for vulnerability factors that interact with matching life events to produce depression. In their review, dependency is reasonably specifically linked with interpersonal loss events in the prediction of depression, but self-criticism is not as specific; research in the sociotropy-autonomy tradition generally finds greater support for a specific vulnerability between sociotropy and interpersonal events, whereas autonomy has been less clearly supported.

However, it is important to note that the empirical support for the congruency model has been broadly based on a variety of cross-sectional and laboratory studies as well as longitudinal studies. Of relevance to the present chapter, relatively few personality/schema-matching studies have included longitudinal designs, optimal methods of stress assessment, and clinical evaluations of unipolar depression (Hammen & Goodman-Brown 1990; Hammen et al. 1985, 1989, 1995; Lam et al. 1996; Segal et al. 1992; see also cross-sectional studies of depressed patients by Mazure et al. 2002, Robins 1990, Spangler et al. 1996). These studies varied in methods of assessing personality vulnerability relevant to the congruency hypothesis and varied in the consistency of results. However, all found some support for the improvement in prediction of depressive reactions to life events by including measures of cognitive or personality vulnerability, and most found support particularly for depression following the matching of interpersonal life events and interpersonal vulnerability. Because the congruency model is one of the most clear diathesis-stress models of depression, and because it has practical treatment and prevention implications, it warrants further study with increasingly sophisticated methods and measures.

Chronic Stress

McGonagle & Kessler (1990) asserted "the near-exclusive emphasis of stress research on life events has been misplaced" (p. 699). There are two reasons to take this assertion very seriously. One is the evidence from these authors' research (McGonagle & Kessler 1990), based on interviews of 1755 respondents, that chronic stress (defined as stress ongoing for more than 12 months) is a stronger predictor of depressive symptoms than acute stressors. The other reason is that failure to assess and evaluate the effects of chronic stress means ignoring a common and obvious source of variability in the stress-depression relationship and obscuring a full understanding of its mechanisms.

Chronic stress has not been ignored entirely in studies of depression, but its definition has varied considerably. For instance, Brown & Harris (1978), defining it as "ongoing difficulties lasting at least 4 weeks," found that cases of depression were substantially likely to have experienced either an ongoing difficulty or at least one severe life event prior to onset. Brown's studies have typically not separated or compared the effects of chronic and acute stress, but Rojo-Moreno et al. (2002) found equal predictability of depression from acute stressors and ongoing difficulties, using the same methods as Brown and colleagues. Other research has found that continuing adverse conditions, such as poverty, medical disabilities, and lasting marital discord, are associated with risk for depression (e.g., Brown & Harris 1978, Bruce & Hoff 1994, Dohrenwend et al. 1992, Swindle et al. 1989). Breslau & Davis (1986) defined chronic stress in women as having a disabled child, and found such experiences to be related to more lifetime episodes of major depression but not to higher rates of current depression in such women compared with nonstressed controls. Chronic stress, defined as absence of social support, also was found to be associated with depression (e.g., Paykel & Cooper 1992).

Hammen and colleagues developed an interview-based chronic stress profile covering domains such as intimate relationships, close friendships, family relations, finances, and the health of self and family members in the past six months. They found, for example, that chronic stress predicted increased depression in patients (Hammen et al. 1992) and depression in youth at risk for depression (Hammen et al. 2004). Mazure (1998) advocates systematic assessment of chronic stress over multiple domains, reasoning that omission of any important domain likely underestimates the true effects of the stress-depression association.

Lack of inclusion of chronic stress assessment has precluded answering several important questions. One is whether chronic stress predicts chronic depression. A review of the limited literature by Riso et al. (2002) suggested such a pattern (see also Hayden & Klein 2001), although Kessler (1997) has noted that the indeterminate nature of the timing of chronic stress and depression makes it difficult to evaluate the causal direction of the relationship. Another question concerns the possible functional relationships between chronic and episodic stress in precipitating depressive episodes. It has been hypothesized that chronic stresses exacerbate the effects of acute stressors on depression (e.g., especially through a process of events "matching" ongoing conditions; Brown & Harris 1978), or that life events magnify the depressive consequences of chronic strains. Interestingly, McGonagle & Kessler (1990) found a negative interaction between chronic and episodic events, such that chronic stress reduced the impact of acute stress on depressive symptoms in a large community sample. Cairney et al. (2003) found similar results in a study of single and married mothers: Life events were stronger predictors of major depression in married mothers compared to single mothers (who had higher levels of chronic stress). These authors explain the results as a "saturation" effect, in which single mothers are less reactive to life events because they are already experiencing high rates of chronic stressors and become accustomed to dealing with them.

Chronic stress is an important area for further study, with significant implications for interpretation of associations between episodic stress and depression. Unresolved empirical questions remain, as do conceptual questions of how chronic and episodic stressors may work together to produce depression, and considerably more effort is needed to refine the definitions and methods of assessment of chronic stress.

THE RELATIONSHIP BETWEEN STRESS AND DEPRESSION: WHAT KIND OF DEPRESSION?

Two significant issues regarding the clinical aspects of depressive disorder continue to raise interesting conceptual questions and stimulate research: (*a*) endogenous versus nonendogenous depression and stress, and (*b*) stress in the prediction of first versus later onsets of depression.

Endogenous Versus Nonendogenous Depression and Stress

The question of an association between endogenous and nonendogenous depressions and stress precipitation, once a topic of interest to researchers attempting to identify depression subtypes that reflected psychogenic versus biological etiologies, has generated relatively little research in the past ten years. Two approaches predominated in earlier research on possible stress-reactive types of depression: (*a*) those studies that defined groups differing on presence or absence of stressors prior to a depressive episode, and examined their endogenous versus nonendogenous symptom patterns, and (*b*) studies that identified groups differing on endogenous/nonendogenous symptom patterns and determined whether they experienced a precipitating stressor. This research has been reviewed in Hammen (1995) and Mazure (1998), indicating mixed findings but overall more consistent agreement that stressors were as likely to be associated with depressions defined by endogenous symptoms as nonendogenous symptoms (e.g., Bebbington et al. 1988, Zimmerman et al. 1986). A notable exception was a study by Frank et al. (1994), who found that research diagnostic criteria–defined endogenous depressives were less likely to have had a provoking stress prior to onset (43%), compared to nonendogenous depressives (65%). Brown et al. (1994) found no differences among those with first onset, but did find less likelihood of a provoking stress among those with endogenous symptoms compared to nonendogenous among patients with a history of recurrent depression.

The research on this topic has been greatly limited by variations in criteria used to define endogenous and nonendogenous depression, by potentially confounding and largely unexplored differences in ages of groups (e.g., endogenous symptoms may be more likely among older patients who generally report less stress), and of course, by differences in measurement of stressful life events. In part to avoid the misleading implication of the term "endogenous" as signifying absence of stress precipitation, the more recent versions of the *Diagnostic and Statistical Manual* (DSM-IV, DSM-IV-TR; American Psychiatric Association 1994, 2000) have defined a "melancholic" subtype entirely in terms of qualitative symptoms. While the ultimate validity of such subtypes for different etiological models and treatments remains to be determined, it seems fruitful to pursue factors other than presumed subtypes to explain possible differential susceptibility to the precipitating effects of stressful life events on depression.

First Versus Later Onsets of Depression

There are conceptual and practical reasons for paying close attention to the distinction between first and later episodes and their association with stressors. Kessler (1997) is among many who have noted that most studies about depression are about depression recurrence since relatively few among a sample of depressed people will be experiencing their first episode, and that predictors of first and later episodes are likely to be different (e.g., Daley et al. 2000). Furthermore, failure

to control for or otherwise account for prior history of depression will potentially lead to erroneous conclusions. Prior depression may alter the probability or nature of life event occurrence (as discussed below in the Stress Generation section), and the association of stress and depression may vary across the course of repeated episodes (discussed in the Kindling/Sensitization hypothesis section below).

The great majority of studies of the association between major depression and stressful life events have not distinguished between first and recurrent episodes. However, stimulated by Post's (1992) kindling/sensitization model that neurobiological changes associated with mood disorder episodes and stressors will lead to increasing independence between stress and episodes, several studies have specifically addressed the issue of stress-depression associations in first versus recurrent episodes of unipolar depression. Approximately ten studies were located that have addressed the issue comparing first versus recurrent depression in unipolar depressed samples (see review in Mazure 1998, Daley et al. 2000 and Lewinsohn et al. 1999 on adolescents, and Ormel et al. 2001 on later life depression). About half the studies do find support for higher rates of stressors prior to first onset compared to later onset, but the other studies do not. Most of the studies include interview measures of episodic stressors, but other methodological difficulties obscure conclusions, including some studies that contain bipolar patients, and varying definitions of stressors and time frames. Importantly, the great majority of the studies have not controlled for gender or age, which may affect the rates of stressors (e.g., female and younger patients typically report higher rates of stressors). Moreover, none of the studies measured or controlled for chronic stress. It is possible that high levels of chronic stress play a role in recurrence separate from, or in interaction with, episodic stressors—but if a major form of stress is unmeasured, the overall impact of stress on depression appears to be attenuated. Perhaps of most concern to the first-onset hypothesis is that none of the studies had a within-person design, which is the critical test of the hypothesis. Furthermore, as Ormel et al. (2001) point out, comparing different groups with first onset or recurrences does not deal with the problem that those with recurrences are the vulnerable individuals who may have had depressive reactions even to mild events and who may get depressed before a severe stressor happens to them. In view of the empirical and methodological limitations, therefore, the first- versus later-episode stress phenomenon remains an intriguing hypothesis rather than an established fact. The following section presents further discussion of the kindling/sensitization hypothesis.

THE RELATIONSHIP BETWEEN STRESS AND DEPRESSION: WHAT KIND OF RELATIONSHIP?

As noted above, there is strong accumulated evidence that episodic stressors play a causal role in many instances of major depression. Testing for the strength of this association was the goal of research on this topic in the first couple of decades

in the history of the field. However, recently there has been increasing awareness of, and interest in, a more dynamic, transactional view of the stress-depression association, including the changing relationship between stress and depression over time, as well as the effect of depression and depression vulnerability on the occurrence of stress.

Kindling/Sensitization and the Changing Relationship of Stress and Depression

Stimulated by Post and colleagues (Post 1992, Post et al. 1984), there has been growing interest in the hypothesis that recurrent episodes of mood disorders may become progressively independent of stressors, as a function of neurobiological changes associated with repeated stressors and repeated episodes that render the person sensitized or "kindled," and thus likely to experience spontaneous episodes. A key empirical element of the hypothesis, reviewed above, is the purported greater association of stressful life events with the initial depressive episode compared to later episodes. Comparing first versus later episodes in different groups of individuals does not truly address the kindling hypotheses, however, because those who are most vulnerable to recurrent episodes may have always been more sensitive. Therefore, employing the critical within-person design permits evaluation of a person's own individual pattern over time of the association between stressors and depressive episodes. Such a study was undertaken by Kendler et al. (2000), who studied nearly 2400 female twins over four waves, each separated by at least 13 months. Using diagnostic assessments based on the Structured Clinical Interview for DSM-IV and life-event interviews based on Brown's (Brown & Harris 1978) long-term contextual threat scoring methods, they computed both between-subjects and within-subjects analyses of the interaction between previous number of episodes and life events occurring prior to the targeted most recent episode. They found evidence in both types of analyses for kindling effects, with a diminishing association between life events and depression with increasing numbers of prior episodes (up to 6–8 episodes). Controlling for severity ratings of the events did not alter the pattern. Kendler et al. (2000) suggest that whatever effect is involved—whether biologically or psychologically mediated—it appears to occur intensively in the first few episodes after initial onset, and then the kindling process slows or stops. Similar within-subject patterns were reported among a subgroup of patients studied by life-charting methods by Ehnvall & Agren (2002).

Further analyses by Kendler and colleagues indicated that the kindling pattern was strongest in those at low genetic risk for depression (Kendler et al. 2001a). In contrast, there was only a weak association between stressful life events and depression in those at genetic risk. Such individuals had a pattern the authors termed "prekindled," with an association between stress and depression that was similar to those at low genetic risk who had already experienced three depressive episodes. Thus, the results suggest two different pathways to a kindled or sensitized state in which episodes occur with little or no stress precipitants: through the experience of

multiple episodes in the low-genetic-risk group, or through heritability of high risk for depression. Further studies are needed to confirm the patterns in longitudinal studies, and, of course, to clarify the nature of the mechanisms that account for the kindling/sensitization effect. It should be noted that none of the studies cited measured chronic stress, and such omission may obscure the nature of associations between clinical history, episodic stress, and depression.

Stress Generation

Stress researchers have often noted the likelihood that depression contributes to the occurrence of stressful life events, but have generally approached the issue as a methodological problem or a confound in the empirical relationship between stressors and depressive outcomes. More recently, however, the role of the individual's contribution to stress occurrence has attracted attention for conceptual reasons, highlighting the bidirectional association between stress and depression, thus blurring the boundary between diathesis and stress (e.g., Rutter 1986). Attention to the person's role in causing stressors necessitates complex transactional models of depression vulnerability and opens new areas for discovery.

Hammen (1991) used the term "stress generation" to describe the finding that during a one-year follow-up period, a clinical sample of women with histories of recurrent unipolar depression were significantly more likely to experience high levels of episodic life events to which they had contributed ("dependent events"; especially those with interpersonal content, and its subset, conflict content), compared to women with bipolar disorder, medical illness, or no disorder. The stress generation finding has been replicated among those with histories of major depression, including community samples of late adolescent women (Daley et al. 1997), adolescent males and females (Hammen & Brennan 2001, Patton et al. 2003), adult men (Cui & Vaillant 1997) and women (Hammen & Brennan 2002, Harkness & Luther 2001), children of depressed mothers (Adrian & Hammen 1993), and clinical samples of children and adolescents (Rudolph & Hammen 1999, Rudolph et al. 2000) and adults (Harkness et al. 1999). Most of these studies found that elevated rates of stressors among those with depression histories did not occur for independent (fateful) events, and were specific to dependent events that are especially likely to reflect interpersonal content.

There are significant implications of the higher rates of event occurrence among depressed individuals. Clinically, exposure to elevated rates of stressors likely predicts recurrences of depression in a self-perpetuating cycle of depression and stress. Moreover, interpersonal, dependent stressors may be especially likely to predict depressive episodes (e.g., Hammen et al. 1985, Kendler et al. 1999). Thus, an understanding of the correlates and mechanisms of stress generation would likely shed light on an important aspect of vulnerability to recurrent depression and yield treatment implications for possible prevention of recurrences.

What factors contribute to stress generation? Elevated levels of stressors do not appear to be due solely to depressive symptoms. Although it is doubtless true that

the pessimism, irritability, low energy, and anhedonia of depression may contribute to relationship difficulties, several studies have found that elevated rates of negative interpersonal events occur even in periods of remission (e.g., Daley et al. 1997, Hammen 1991, Hammen & Brennan 2002; see also Kendler & Karkowski-Shuman 1997). Thus, the depression syndrome itself may not account for the elevated rates of interpersonal and dependent events occurring between episodes.

Hammen (e.g., 1992, 2003; Hammen & Brennan 2002) has emphasized the idea that depressed women are often locked into highly stressful family environments that include marital discord, husbands who have high rates of psychological disorders, and children who themselves display elevated rates of depression, anxiety, and disruptive disorders. The potential for conflict, loss, and disruption events occurring within such family contexts seems high indeed. Women who live in such environments may experience stressful events in their relations within their social networks even if they themselves are not currently depressed. A number of factors that may contribute to dysfunctional mate selection and interpersonal difficulties with spouses and children may be speculated to underlie the creation of stressful family contexts, and are discussed further below. Similarly, socially disadvantaged (e.g., low-income, low-education, ethnic minority) environments confer increased risk for life event occurrence; Fergusson & Horwood (1987), for example, found evidence supporting this hypothesis among a community sample of women in a longitudinal study, although the investigation did not evaluate depression status.

Kendler and colleagues have promoted a somewhat similar idea that depressed individuals "select themselves into" problematic environmental contexts (e.g., Kendler et al. 1999). In several studies of twins, these investigators found evidence of heightened experience of stressors among those with histories of major depression. They also found that elevated rates of life events appear to be genetically mediated (Kendler & Karkowski-Shuman 1997, Kendler et al. 1999; see also McGuffin et al. 1988 and Kendler et al. 1993b for further evidence consistent with genetic transmission of greater exposure to stressful life events among families with depressed members). Kendler & Karkowski-Shuman (1997) found high levels of interpersonal (including serious marital) events, as well as financial events, among those with depression histories.

Several studies have explored individual difference predictors of stress generation, including clinical and personality/behavioral variables. Daley et al. (1997) found that depression with comorbidity was associated with higher levels of dependent events (especially conflict-themed events) over a one-year follow-up compared with depression alone or no disorder. Daley et al. (1998) also found that Axis II symptomatology [especially Cluster A (schizoid, paranoid, schizotypal) and Cluster B (antisocial, borderline, histrionic, and narcissistic) symptoms] contributed to stress generation in the same sample. Harkness & Luther (2001), in their cross-sectional analysis, also found that major depression comorbid with dysthymia or anxiety disorders was associated with higher levels of dependent events. Harkness et al. (1999) found that depressed outpatients with recurrent depression reported significantly more dependent events in the past year than did first-onset

depressives, which suggests the possibility of a progressive stress-generation effect.

The pattern of elevated interpersonal life events associated with history of depression lends itself to the exploration of experiences and personal characteristics that impair interpersonal functioning. Hammen et al. (1992) speculated that parental psychopathology would lead to impairment of interpersonal functioning likely through maladaptive parenting, and found that family history of psychopathology indeed predicted elevated rates of stressors among depressed outpatients (although actual interpersonal functioning was not directly assessed). Adrian & Hammen (1993) found similar patterns for elevated interpersonal stressors among children of depressed mothers. Daley et al. (1997) pursued a similar topic but found that the effect of parental disorder on women's episodic life stress was mediated through the person's own psychological disorder. Hammen et al. (2004) recently found support for a model in which maternal depression contributes to adolescents' stressful life events through various routes including negative parent-child relations and the mothers' own dysfunctional relations with partner, friends, and extended family. Thus, it seems likely that a key component of stress generation is maladaptive family background, presumably operating via both genetic and social interactional processes.

Several studies have specifically attempted to test the contribution to stress generation of dysfunctional social problem-solving skills. Davila et al. (1995) found that poor interpersonal problem-solving skills based on responses to hypothetical scenarios predicted later occurrence of interpersonal stress in a longitudinal study. However, Segrin (2001) found only weak support for an association between self-reported social skills and negative life events. In contrast, Herzberg et al. (1998) found that lower self-reported interpersonal competence (particularly lower levels of provision of emotional support to others) predicted increased chronic interpersonal stress a year later, even when prior psychopathology was controlled. Davila et al. (1997) found a pattern of marital stress generation in which dysphoric women created stress in their marital relationships (and more depression) over time, accounted for largely by negative expectations of support from spouses and by negative patterns of solicitation, reception, and provision of support in interactions with their husbands. The construct of reassurance-seeking (habitual and excessive bids to get reassurance from others of their caring) is an example of a specific maladaptive interpersonal skill that has been found to predict the occurrence of subsequent minor stressors, which in turn predict increased depressive symptoms (Potthoff et al. 1995). Daley et al. (1997) also tested traits related to interpersonal functioning, sociotropy, and autonomy; they found that autonomy, but not sociotropy, predicted subsequent increases in dependent and conflict stress when current symptomatology was controlled. Autonomy reflects high valuing of achievement, independence, self-reliance, and assertiveness that might be distancing and abrasive in some interpersonal contexts. Additionally, several studies have implicated traits of both dependency and self-criticism in the generation of stressful life events; for a review see Zuroff et al. (2004).

A potentially important predictor of stress generation is the neuroticism trait. Kendler et al. (1999, Kendler & Karkowski-Shuman 1997) suggest that neuroticism or "difficult temperament" may be one of the genetically transmitted traits that predisposes to both stressful life events and depression, or to sensitivity to respond to stressors with depression (Kendler et al. 1995, 2003). Kendler et al. (2003), for example, found that neuroticism was a strong predictor of stressful life events, particularly those related to interpersonal relationships (see also Fergusson & Horwood 1987, Poulton & Andrews 1992). In other analyses, Kendler et al. (2004) found that neuroticism moderated the effects of stress on depression, particularly potentiating its effects at the highest levels of stress exposure, thus completing the link between neuroticism, generation of stressful events, and depressive reactions to stressors.

Full understanding of the predictors of a person's contributions to the occurrence of interpersonal, dependent stressors is limited at this point. Further work is needed to explore patterns of mate selection and parenting that might result from various interpersonal vulnerabilities and in turn create stressful contexts that require excellent skills to manage, but that commonly eventuate in repeated stressors. In addition, there are doubtless many traits and behavioral patterns that either cause conflicts and disruptions or reflect inadequate coping with such circumstances in order to prevent them from becoming severe episodic events. Finally, stress-generation processes likely reflect both cognitive (e.g., Simons et al. 1993) and biological vulnerabilities that affect a person's interpretations of situations and their consequences, and the threshold of activation of depression-related neurocognitive and neurohormonal reactions.

THE STRESS-DEPRESSION RELATIONSHIP: MODELS, MODERATORS, AND MEDIATORS

The purpose of this final section is to identify recent empirical and conceptual developments in the effort to explain the relationship between stress and depression. These developments address why some individuals become depressed and others do not following exposure to stress, and how such outcomes may occur. The purpose of this section is not to evaluate the success of different diathesis-stress models of depression, but rather to note issues that might help to take stock of where we are and where the field is going.

One of the most striking developments is the orientation toward increasingly complex, multifactorial models, including those in which the boundaries between diathesis and stress are blurred owing to the contributions of the diatheses to the occurrence of stress (e.g., Dohrenwend et al. 1996; Hammen et al. 2004; Kendler et al. 1993a, 2002; Zuroff et al. 2004; to name a few). Many of the comprehensive models include all or most of the following elements: biological, developmental, psychological, and sociodemographic factors with mutual influences among the variables and between depression and the antecedent variables. Recent findings

and approaches in each of these broad areas are reviewed briefly, with the acknowledgment that to date, few investigators have been fully able to empirically test the complex multifactorial models.

Biological Moderators and Mediators

Much has been written recently about the potential role of dysregulation of biological stress processes as a cause of depression. Abnormalities of the hypothalamic pituitary adrenal (HPA) axis have been speculated to play a critical role in development of depressive symptoms, persistence of symptoms, and recurrence of depression (e.g., reviewed in Gold et al. 1988, Holsboer 1995, Plotsky et al. 1998, Thase et al. 2002). For instance, most models speculate about dynamic, progressive HPA abnormalities such that traumatic stress or chronic stress not only triggers behaviors and emotions related to depression and anxiety, but also might result in prolonged cortisol hypersecretion and possibly eventually to hippocampal atrophy due to neuronal death (Lee et al. 2002). Widespread neuronal circuitry connecting corticotrophin-releasing factor with brain structures essential to cognitive and emotional processing, and its interactions with other neurotransmitter systems in the brain, provides an integrative approach to the diverse biological mechanisms implicated in the pathophysiology of depression.

In recent years there has been an additional emphasis on the role of early exposure to childhood adversity, trauma, and abuse in promoting abnormalities of HPA axis activity that result in sensitization to the effects of later stressors (e.g., reviewed in Heim & Nemeroff 2001, Kaufman et al. 2000, Ladd et al. 2000). Numerous preclinical studies, as well as a growing body of human research, especially on maltreated infants and children (Cicchetti & Toth 2005), have provided some evidence of cortisol and other HPA abnormalities under high stress conditions. However, despite dozens of studies indicating that laboratory-based social stress results in elevated cortisol (e.g., Dickerson & Kemeny 2004), there are scant data on the neuroendocrine correlates of exposure to naturally occurring stressors and their association with depressive reactions. A rare exception is a longitudinal study by Harris et al. (2000), who examined morning and evening cortisol levels and onset of depressive episodes following severe stressors or ongoing difficulties among women considered to be at risk or low risk for depression (due to negativity in their primary relationships or to low self-esteem). Harris et al. (2000) found that higher morning (but not evening) cortisol level, life events, and vulnerability status all predicted depression onset (but they did not test for interactions); Goodyer et al. (2000) found similar results with adolescent depression. Morning cortisol levels were independent of vulnerability status or history of previous psychiatric episodes, and therefore did not appear to be consequences of prior depression. The authors speculate that high cortisol levels might make the brain more susceptible to depression in the face of stress, but the specific mechanisms are not known.

Contrasting with the findings of Harris et al. (2000), Strickland et al. (2002) examined basal cortisol levels in depressed and nondepressed women and their association with recent stressors. Counter to the hypotheses, depression was not

associated with elevated cortisol, but evening cortisol was elevated in the presence of recent life events. The authors note that results probably vary by level of chronic stress and extent of anxiety symptoms. Indeed, this emerging field of cortisol/stress associations with depression seems to be marked by inconsistent or unexpected results (e.g., Young et al. 2000), as well as conceptual uncertainty over the specific pathways to depressive versus anxiety outcomes, and the distinction between post-traumatic stress disorders and mood disorders. Further understanding of the biological stress processes will move the field forward, but considerable work also is needed to integrate the biological paradigms with data on stressful life events and risk for depression.

Developments in genetic contributors to depression also have important implications for understanding the association between stressors and depression. Behavioral genetic studies with twin populations have established evidence of moderate heritability of risk for depression, and specifically, a gene by life stress interaction in predicting depressive reactions to stressors (Kendler et al. 1995). For instance, Kendler and colleagues demonstrated fit for a model, tested among female twin pairs, indicating that genetic factors affected sensitivity to severe stressors and resulted in depressive episodes; the effects of severe stressors were substantially greater among those at high genetic risk for depression than among those at low risk.

In a recent New Zealand longitudinal sample, Caspi et al. (2003) found that a polymorphism (short allele) in the promoter region of the serotonin transporter (5-HTTLPR) gene predicted depression in interaction with major stressors. That is, presence of this genetic characteristic moderated the likelihood of reacting to a major stressor with depression, suggesting that an etiological pathway related to serotonergic neurotransmission exists. The Caspi et al. (2003) study was the first to identify a specific genetic locus associated with depressive reactions to stressful life events. The 5-HTTLPR gene has been shown in some studies to be associated with traits generally termed "neuroticism" (Schinka et al. 2004, Sen et al. 2004), which may manifest behaviorally in processes involved in the generation of interpersonal stressors as well as reactions to stressors (e.g., Kendler et al. 2003). Further research is needed to confirm the association of the serotonin transporter gene with trait neuroticism, but the initial genetic studies noted above suggest that one mechanism linking stress with depression concerns biological processes underlying negative affectivity and emotional lability in response to stress.

Developmental Moderators and Mediators

There has been extensive recognition of the contribution of childhood stressful experiences to adolescent and adult depression. The literature on the effects of childhood parental death, divorce and marital discord, parental mental illness and substance abuse, exposure to family violence, neglect, and sexual and physical abuse is too extensive to review here. Kessler & Magee (1993) investigated the power of eight retrospectively reported childhood adversities occurring through age 16 to predict depression in an epidemiological sample, and found that many

were associated with the incidence and recurrence of major depressive disorder by age 20 (also, most are not unique or specific to depression: Kessler et al. 1997).

Does exposure to childhood or lifetime adversity play a role in the response of such affected individuals to stressful life events in adulthood? The early work of Brown & Harris (1978) indicated that the effect of recent stressful life events and ongoing difficulties was moderated or potentiated in part by the loss of a mother in childhood. Increasingly, stress researchers have specifically called for inclusion of lifetime (especially childhood) exposure to stressful events and circumstances as possible moderators or mediators of the effects of proximal stress on depression (or some view proximal stressors as the moderators or mediators of the effects of early adversity). Ensel & Lin (1996) examined the role of "distal" stressors (defined in their study as those occurring up to 15 years ago in their longitudinal study), and found that such events had direct predictive effects on current depressive symptoms, about equal to the effects of proximal (prior year) negative events (see also Garnefski et al. 1990).

One effect of early adversity might be its association with higher levels of adult stress. Bifulco et al. (2000) found that women who had experienced neglect or abuse in childhood had higher adult levels of severe adverse events and chronic stressors (especially in close relationships) than did those who did not have such experiences. In their study, the combination of childhood abuse/neglect and high levels of adult exposure to negative life events best predicted recurrent depressive episodes. Relatedly, Kessler & Magee (1994) found that chronic interpersonal stress in adulthood mediated the association between exposure to family violence in childhood and adult depression. Kendler et al. (1993a) found that lifetime history of traumas indirectly predicted risk for major depression, occurring both through an effect on prior episodes predicting current depression and through traumas predicting higher levels of recent stressors and ongoing difficulties.

Another approach to the effects of early adversity on later reactions to stress has postulated a "sensitization" effect. Hammen et al. (2000) tested the hypothesis that exposure to childhood adversities (defined by the Kessler & Magee 1993 list) would moderate the association between recent stressful life events and depressive episodes, specifically predicting a "sensitization" effect such that early-stressed women would have less stress prior to onset than women without early adversity. Support for the prediction was found in a longitudinal study of late adolescent women, suggesting that it takes less stress to precipitate major depressive episodes in women exposed to childhood adversities compared with those not exposed. Caspi et al. (2003) found that genetic factors (presence of the 5-HTTLPR short allele) moderated the effects of early childhood maltreatment on young adult depression. Maltreatment had little effect on the presence of depression unless the individual carried one, or especially two, short alleles. As noted above, the investigators found that the presence of these genes moderated the effect of stressful life events on major depressive episodes, but they did not report tests of the associations among maltreatment, adult stressors, genetic effects, and depression.

Overall, therefore, this selective review suggests that early or distal stressors may have an important impact on later reactivity to stress, possibly in part by increasing chronic and episodic stress burden or in part by reducing the threshold at which stressors precipitate depression. There has been considerable research and speculation about other mechanisms (e.g., biological, attachment bonds, and cognitive "working models") linking early parent-child relationship quality to vulnerability to later depression, usually with an implicit hypothesis that adult stressors trigger the underlying vulnerability (e.g., reviewed in Goodman 2002, Meyer et al. 2001; also see Cicchetti & Toth 2005). Further research based on refined methods of measuring early and lifetime stress exposure is needed to help clarify the possible cumulative vulnerability to stress across the life span, and to advance understanding of the processes by which such vulnerability eventuates in depression.

Psychological Moderators and Mediators

There has been a great deal of interest in psychological characteristics that moderate the stress-depression relationship, including cognitive styles reflecting typical but dysfunctional interpretations of the self and events, values and goals such as sociotropy/autonomy, and traits such as perfectionism and neuroticism.

The cognitive vulnerability model of depression has stimulated considerable research and elegant hypotheses (e.g., reviewed in Abramson et al. 2000), but remarkably, relatively few studies actually tested a diathesis-stress model with clinically significant depressive outcomes and stressful life event assessments in adult samples. Most research on cognitive diatheses, for instance, even when including prediction of depressive diagnoses, has generally failed to include or test for effects of stressors and their interactions with vulnerability, or have not yet reported results of such tests. One exception, predicting major depression in adolescents, tested stress (via questionnaire) by dysfunctional attitudes or negative attribution style interactions (Lewinsohn et al. 2001). The investigators found support for the predicted patterns with the dysfunctional attitudes (high stress plus high dysfunctional attitudes scores were associated with increased risk of developing a major depressive episode), but less support for attribution style (at high levels of stress, negative attribution style had little effect on outcome, but at low levels of stress, higher rates of depression occurred at higher levels of negative attribution style). Further exceptions to the paucity of cognitive diathesis-stress tests include several studies that were noted in the section above on content by personality/cognitive vulnerability congruence. The studies generally lend support to the hypothesis that interpersonal vulnerability, as conveyed by measures of attitudes and beliefs about the self in relationships and importance to the self of social connectedness, predicts depression following stressful life events with interpersonal content.

Additional noteworthy cognitive-diathesis studies of diagnosed depression include tests of a self-esteem vulnerability model by Brown and colleagues (Bifulco et al. 1998, Brown et al. 1990, Brown & Harris 1978, Harris et al. 2000), in which low self-esteem is measured by interviewer ratings from subjects' comments about

their personal attributes, role competencies, and general self-acceptance. These studies have generally found support for the prediction that low self-esteem coupled with the experience of severe stressors triggers depressive episodes in community samples of women.

Several recent studies have investigated the question of whether trait neuroticism is a diathesis for depressive outcomes in the face of stress. As previously noted, Kendler et al. (2004) found that neuroticism moderated adults' reactions to stressful life events (and contributed to the occurrence of stressful life events; e.g., Kendler et al. 2003, Poulton & Andrews 1992). Van Os & Jones (1999) found that childhood-assessed neuroticism contributed to sensitivity to stressful life events in adulthood. A venerable topic in depression research in past decades, neuroticism appears to be emerging again as a significant variable in stress-depression research, perhaps largely because of its implications for understanding stress generation and stress reactivity, and as a candidate for aspects of genetic risk for depression.

Sociodemographic Moderators and Mediators

Considerable research has addressed issues involving how stressors and their impact on depression may vary with constructs that reflect broad elements of an individual's social and demographic roles and contexts, including poverty and disadvantage, social support, and gender. Gender is the focus of this section. Any viable model of depression must address the well-known preponderance of female to male depression onsets, and there has been increasing interest in the issue of whether one element in the gender difference in rates of depression may be women's greater exposure to stressors—and possibly, greater reactivity to stressors.

Three classes of stress exposure have received some attention: specific stressors such as sexual victimization, chronic stress, and episodic stress. It has often been noted that females are substantially more likely to be victims of traumatic experiences such as sexual abuse and assault than are males, and that such experiences, especially in childhood or adolescence, are commonly predictive of depressive episodes (e.g., Cutler & Nolen-Hoeksema 1991, Weiss et al. 1999, Whiffen & Clark 1997). Cutler & Nolen-Hoeksema (1991), for instance, hypothesized that at least 35% of the gender difference in rates of depression could be due to the higher incidence of women's exposure to sexual assault. If other forms of assault with higher exposure rates among women, such as serious marital violence, are factored in, Nolen-Hoeksema (2002) speculates that even more of the variance in gender differences might be accounted for. As noted above, childhood exposure—and perhaps especially abuse—may create biological and psychological changes in stress-response mechanisms that increase the probability of depressive reactions to later stressor exposure.

Chronic stress, as noted above, has been inconsistently defined and relatively less studied among stress researchers. However, if measured as poverty and single parenting, women's rates of chronic stressful conditions exceed those of men, and these circumstances are often associated with depression (e.g., Brown & Moran

1997, Bruce et al. 1991). Experiencing chronic illness and serving as primary caretakers for ill relatives also appear to be circumstances experienced by more women than men, and such conditions are also associated with depression (e.g., Maciejewski et al. 2001). Finally, Nolen-Hoeksema et al. (1999) assessed female role-related "chronic strains" in the form of reduced power and decision making, such as lack of affirmation in close relationships, role burden, housework inequities, childcare inequities, and other parenting strains. They found that such strains predicted depression over time and partially mediated gender differences in depression. It would be important to explore how chronic strains unique to women's lives might operate together with episodic stressors to precipitate depressive disorders.

Several recent studies have addressed the question of whether women experience higher rates of episodic stressful life events than do men. Mazure (1998) points out that most studies of stress and depression have been conducted with women, precluding tests of differential exposure and reaction to stressors. McGonagle & Kessler (1990) found marginally significantly more content domains of acute stress in women than in men, although they did not count the total numbers of stressors. Maciejewski et al. (2001) found no gender differences in the number of recent acute stressors in a large community sample of adults. Kendler et al. (2001b) also did not find overall different rates of acute events in a large twin sample but noted that men had higher frequencies of job loss, legal problems, and work problems, whereas women had higher rates of housing problems, loss of confidants, and problems getting along with individuals in their networks. However, several investigators have found significantly higher rates of total episodic stressors in adolescent girls compared to boys, and the effect was especially apparent for girls' higher rates of interpersonal events (Ge et al. 1994 and Rudolph & Hammen 1999, regarding adolescents; Spangler et al. 1996, regarding depressed adult outpatients). Although more comparison studies need to be conducted, it may be that the overall rate of exposure to acute stressors is not different, whereas specific domains such as interpersonal events may be especially common among females.

The issue of gender differences in depressive reactions to stress appears to yield greater consensus, with more studies indicating that women are more likely to become depressed in response to stressors than are men. McGonagle & Kessler (1990) found no sex difference in the impact of episodic stress on depressive symptoms, but the effect of chronic stress was twice as strong in women as in men across various content domains.

Kendler et al. (2001a) found specific differences in genders according to which events were depressogenic: for men, divorce, separation, or work problems; for women, problems in relationships with people in their close networks. Kendler et al. (2001a) argued that gender differences in depression were not explained by differential sensitivity to stressors. Maciejewski et al. (2001) found that although women did not have higher rates of stressors, they were more likely to become depressed in response to life events (controlling for a number of factors including socioeconomic status, age, marital status, history of depression, chronic health problems, and other chronic stressors). Illustrating women's greater reactivity,

Maciejewski et al. (2001) noted that there were a few events to which both genders were equally reactive (e.g., death of spouse or child, divorce, or marital problems), but women were also more reactive to deaths in a broader range of relationships, such as friends and relatives. Van Os & Jones (1999) also found that women were more vulnerable to depression in the face of stressors. Rudolph (2002, Rudolph & Hammen 1999) found that adolescent girls were more likely to experience depression associated with interpersonal events than were boys. Spangler et al. (1996) found that women were more likely to have a diathesis-stress match (especially interpersonal) prior to depression onset than were men.

Overall, findings of gender differences in exposure to stress, and especially reactivity to stress, may provide clues to the greater rates of depression in women. However, the mechanisms underlying such patterns remain to be explicated, and several theoretical reviews have offered a variety of hypotheses (e.g., Cyranowski et al. 2000, Hankin & Abramson 2002, Nolen-Hoeksema 2002, Nolen-Hoeksema & Girgus 1994).

CONCLUSIONS AND FUTURE DIRECTIONS

Research has supported a strong association between stress and depression, but the overarching question remains: Why do some people get depressed following stressful experiences and others do not? Promising explorations of this question from cognitive, developmental, biological, personality, and contextual approaches have been pursued, with much left to be done to resolve the question to the point of yielding treatment and prevention implications. As we build future efforts on previous accomplishments, several challenges are noteworthy.

One fundamental issue is recognition of the empirical limitations of the field: the extent to which most stress-depression research has been based on largely female samples, mostly on episodic stressors, and mainly on cross-sectional designs, with few tests of mediation. Expansion of research populations and longitudinal designs, and conceptualization and measurement of chronic stress, would improve the validity and completeness of our models and their empirical support.

A challenge to the field is the need for multivariate, complex models with different levels of variables, possibly yielding different pathways to depression (e.g., Kendler et al. 2002). Such studies are enormously difficult and require considerable resources, but seem necessary to capture the complexities of the stress-depression process. Such work calls for integrative biological-developmental-psychosocial research, and offers an exceptional opportunity for interdisciplinary efforts.

A further challenge to the field is to characterize and account for the possibility of progressive, changing processes over time and clinical course, and for the mutual and transactional relationships between the person and the environment. Issues such as stress generation, effects of childhood adversity on later susceptibility to stress, onset versus recurrence, and stress sensitization and kindling processes are

all examples of research that deepens our appreciation that a dynamic rather than static process occurs in the stress-depression relationship.

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LITERATURE CITED

Abramson LY, Alloy L, Hankin B, Haeffel G, MacCoon D, Gibb B. 2002. Cognitive vulnerability-stress models of depression in a self-regulatory and psychobiological context. See Gotlib & Hammen 2002, pp. 268–94

Adrian C, Hammen C. 1993. Stress exposure and stress generation in children of depressed mothers. *J. Consult. Clin. Psychol.* 61:354–59

American Psychiatric Association. 1994. *Diagnostic and Statistical Manual of Mental Disorders*. Washington, DC: APA. 4th ed.

American Psychiatric Association. 2000. *Diagnostic and Statistical Manual of Mental Disorders*. Washington, DC: APA. 4th ed., text rev.

Bebbington PE, Brugha T, MacCarthy B, Potter J, Sturt E, et al. 1988. The Camberwell Collaborative Depression Study: I. Depressed probands: adversity and the form of depression. *Br. J. Psychiatry* 152:754–65

Beck AT. 1983. Cognitive therapy of depression: new perspectives. In *Treatment of Depression: Old Controversies and New Approaches*, ed. PJ Clayton, JE Barrett, pp. 265–90. New York: Raven

Bifulco A, Bernazzani O, Moran PM, Ball C. 2000. Lifetime stressors and recurrent depression: preliminary findings of the Adult Life Phase Interview (ALPHI). *Soc. Psychiatry Psychiatr. Epidemiol.* 35:264–75

Bifulco A, Brown GW, Moran P, Ball C, Campbell C. 1998. Predicting depression in women: the role of past and present vulnerability. *Psychol. Med.* 28:39–50

Blatt SJ. 1974. Levels of object representation in anaclitic and introjective depression. *Psychoanal. Study Child* 29:7–157

Breslau N, Davis GC. 1986. Chronic stress and major depression. *Arch. Gen. Psychiatry* 43:309–14

Brown GW, Andrews B, Bifulco AT, Veiel HO. 1990. Self-esteem and depression: I. Measurement issues and prediction of onset. *Soc. Psychiatry Psychiatr. Epidemiol.* 25:200–9

Brown GW, Harris TO. 1978. *Social Origins of Depression*. London: Free Press

Brown GW, Harris TO. 1989. Depression. In *Life Events and Illness*, ed. GW Brown, TO Harris, pp. 49–93. New York: Guilford

Brown GW, Harris TO, Hepworth C. 1994. Life events and endogenous depression: a puzzle reexamined. *Arch. Gen. Psychiatry* 51:525–34

Brown GW, Harris TO, Hepworth C. 1995. Loss, humiliation and entrapment among women developing depression: a patient and non-patient comparison. *Psychol. Med.* 25:7–21

Brown GW, Moran PM. 1997. Single mothers, poverty and depression. *Psychol. Med.* 27:21–33

Bruce ML, Hoff RA. 1994. Social and physical health risk factors for first-onset major depressive disorder in a community sample. *Soc. Psychiatry Psychiatr. Epidemiol.* 29:165–71

Bruce ML, Takeuchi DT, Leaf PJ. 1991. Poverty and psychiatric status: longitudinal evidence from the New Haven Epidemiologic Catchment Area Study. *Arch. Gen. Psychiatry* 48:470–74

Cairney J, Boyle M, Offord DR, Racine Y. 2003. Stress, social support and depression in single and married mothers. *Soc. Psychiatry Psychiatr. Epidemiol.* 38:442–49

Caspi A, Sugden K, Moffitt TE, Taylor A, Craig IW, et al. 2003. Influence of life stress on

depression: moderation by a polymorphism in the 5-HTT gene. *Science* 301:386–89

Cicchetti D, Toth SL. 2005. Child maltreatment. *Annu. Rev. Clin. Psychol.* 1:409–38

Coyne JC, Whiffen VE. 1995. Issues in personality as diathesis for depression: the case of sociotropy-dependency and autonomy-self-criticism. *Psychol. Bull.* 118:358–78

Cui X-J, Vaillant GE. 1997. Does depression generate negative life events? *J. Nerv. Ment. Dis.* 185:145–50

Cutler SE, Nolen-Hoeksema S. 1991. Accounting for sex differences in depression through female victimization: childhood sexual abuse. *Sex Roles* 24:425–38

Cyranowski JM, Frank E, Young E, Shear K. 2000. Adolescent onset of the gender difference in lifetime rates of major depression. *Arch. Gen. Psychiatry* 57:21–27

Daley SE, Hammen C, Burge D, Davila J, Paley B, et al. 1997. Predictors of the generation of episodic stress: a longitudinal study of late adolescent women. *J. Abnorm. Psychol.* 106:251–59

Daley SE, Hammen C, Davila J, Burge D. 1998. Axis II symptomatology, depression, and life stress during the transition from adolescence to adulthood. *J. Consult. Clin. Psychol.* 66:595–603

Daley SE, Hammen C, Rao U. 2000. Predictors of first onset and recurrence of major depression in young women during the 5 years following high school graduation. *J. Abnorm. Psychol.* 109:525–33

Davila J, Bradbury TN, Cohan CL, Tochluk S. 1997. Marital functioning and depressive symptoms: evidence for a stress generation model. *J. Personal. Soc. Psychol.* 73:849–61

Davila J, Hammen C, Burge D, Paley B, Daley SE. 1995. Poor interpersonal problem solving as a mechanism of stress generation in depression among adolescent women. *J. Abnorm. Psychol.* 104:592–600

Dickerson SS, Kemeny ME. 2004. Acute stressors and cortisol responses: a theoretical integration and synthesis of laboratory research. *Psychol. Bull.* 130:355–91

Dohrenwend BP, Levav I, Shrout PE, Schwartz S, Naveh G, et al. 1992. Socioeconomic status and psychiatric disorders: the causation-selection issue. *Science* 255:946–52

Ehnvall A, Agren H. 2002. Patterns of sensitisation in the course of affective illness: a life-charting study of treatment-refractory depressed patients. *J. Affect. Disord.* 70:67–75

Ensel WM, Lin N. 1996. Distal stressors and the life stress process. *J. Community Psychol.* 24:66–82

Fergusson DM, Horwood LJ. 1987. Vulnerability to life events exposure. *Psychol. Med.* 17: 739–49

Finlay-Jones R, Brown GW. 1981. Types of stressful life event and the onset of anxiety and depressive disorders. *Psychol. Med.* 11: 803–15

Frank E, Anderson B, Reynolds CF, Ritenour A, Kupfer DJ. 1994. Life events and the research diagnostic criteria endogenous subtype: a confirmation of the distinction using the Bedford College methods. *Arch. Gen. Psychiatry* 51:519–24

Garnefski N, Van Egmond M, Straatman M. 1990. The influence of early and recent life stress on severity of depression. *Acta Psychiatr. Scand.* 81:295–301

Ge X, Conger RD, Lorenz FO, Simons RL. 1994. Parents' stressful life events and adolescent depressed mood. *J. Health Soc. Behav.* 35:28–44

Gold PW, Goodwin FK, Chrousos GP. 1988. Clinical and biochemical manifestations of depression: relation to the neurobiology of stress II. *N. Engl. J. Med.* 319:348–53

Goodman SH. 2002. Depression and early adverse experiences. See Gotlib & Hammen 2002, pp. 245–67

Goodyer IM, Herbert J, Tamplin A, Altham PME. 2000. Recent life events, cortisol, dehydroepiandrosterone and the onset of major depression in high-risk adolescents. *Br. J. Psychiatry* 177:499–504

Gotlib IH, Hammen CL, eds. 2002. *Handbook of Depression*. New York: Guilford

Hammen C. 1991. Generation of stress in the

course of unipolar depression. *J. Abnorm. Psychol.* 100:555–61

Hammen C. 1992. Life events and depression: the plot thickens. *Am. J. Community Psychol.* 20:179–93

Hammen C. 1995. Stress and depression: research findings on the validity of an endogenous subtype of depression. *Dir. Psychiatry* 15:1–8

Hammen C. 2003. Interpersonal stress and depression in women. *J. Affect. Disord.* 74:49–57

Hammen C, Brennan PA. 2001. Depressed adolescents of depressed and nondepressed mothers: tests of an interpersonal impairment hypothesis. *J. Consult. Clin. Psychol.* 69:284–94

Hammen C, Brennan PA. 2002. Interpersonal dysfunction in depressed women: impairments independent of depressive symptoms. *J. Affect. Disord.* 72:145–56

Hammen C, Burge D, Daley SE, Davila J, Paley B, Rudolph KD. 1995. Interpersonal attachment cognitions and prediction of symptomatic responses to interpersonal stress. *J. Abnorm. Psychol.* 104:436–43

Hammen C, Davila J, Brown G, Ellicott A, Gitlin M. 1992. Psychiatric history and stress: predictors of severity of unipolar depression. *J. Abnorm. Psychol.* 101:45–52

Hammen C, Ellicott A, Gitlin M, Jamison KR. 1989. Sociotropy/autonomy and vulnerability to specific life events in patients with unipolar depression and bipolar disorders. *J. Abnorm. Psychol.* 98:154–60

Hammen C, Goodman-Brown T. 1990. Self-schemas and vulnerability to specific life stress in children at risk for depression. *Cogn. Ther. Res.* 14:215–27

Hammen C, Henry R, Daley SE. 2000. Depression and sensitization to stressors among young women as a function of childhood adversity. *J. Consult. Clin. Psychol.* 68:782–87

Hammen C, Marks T, Mayol A, DeMayo R. 1985. Depressive self-schemas, life stress, and vulnerability to depression. *J. Abnorm. Psychol.* 94:308–19

Hammen C, Shih JH, Brennan PA. 2004. Intergenerational transmission of depression: test of an interpersonal stress model in a community sample. *J. Consult. Clin. Psychol.* 72: 511–22

Hankin BL, Abramson LY. 2002. Measuring cognitive vulnerability to depression in adolescence: reliability, validity and gender differences. *J. Clin. Child Adolesc.* 31:491–504

Harkness KL, Luther J. 2001. Clinical risk factors for the generation of life events in major depression. *J. Abnorm. Psychol.* 110:564–72

Harkness KL, Monroe SM, Simons AD, Thase M. 1999. The generation of life events in recurrent and non-recurrent depression. *Psychol. Med.* 29:135–44

Harris TO, Borsanyi S, Messari S, Stanford K, Cleary SE, et al. 2000. Morning cortisol as a risk factor for subsequent major depressive disorder in adult women. *Br. J. Psychiatry* 177:505–10

Hayden EP, Klein DN. 2001. Outcome of dysthymic disorder at 5-year follow-up: the effect of familial psychopathology, early adversity, personality, comorbidity, and chronic stress. *Am. J. Psychiatry* 158:1864–70

Heim C, Nemeroff CB. 2001. The role of childhood trauma in the neurobiology of mood and anxiety disorders: preclinical and clinical studies. *Biol. Psychiatry* 49:1023–39

Herzberg DS, Hammen C, Burge D, Daley SE, Davila J, Lindberg N. 1998. Social competence as a predictor of chronic interpersonal stress. *Pers. Relat.* 5:207–18

Holsboer F. 1995. Neuroendocrinology of mood disorders. In *Psychopharmacology: The Fourth Generation in Progress*, ed. FE Bloom, DJ Kupfer, pp. 957–69. New York: Raven

Kaufman J, Plotsky PM, Nemeroff CB, Charney DS. 2000. Effects of early adverse experiences on brain structure and function: clinical implications. *Biol. Psychiatry* 48:778–90

Kendler KS, Gardner CO, Prescott CA. 2002. Toward a comprehensive developmental model for major depression in women. *Am. J. Psychiatry* 159:1133–45

Kendler KS, Gardner CO, Prescott CA. 2003.

Personality and the experience of environmental adversity. *Psychol. Med.* 33:1193–202

Kendler KS, Karkowski LM, Prescott CA. 1998. Stressful life events and major depression: risk period, long-term contextual threat and diagnostic specificity. *J. Nerv. Ment. Dis.* 186:661–69

Kendler KS, Karkowski LM, Prescott CA. 1999. Causal relationship between stressful life events and the onset of major depression. *Am. J. Psychiatry* 156:837–48

Kendler KS, Karkowski-Shuman L. 1997. Stressful life events and genetic liability to major depression: genetic control of exposure to the environment? *Psychol. Med.* 27:539–47

Kendler KS, Kessler RC, Neale MC, Heath AC, Eaves LJ. 1993a. The prediction of major depression in women: toward an integrated etiologic model. *Am. J. Psychiatry* 150:1139–48

Kendler KS, Kessler RC, Walters EE, MacLean C, Neale MC, et al. 1995. Stressful life events, genetic liability, and onset of an episode of major depression in women. *Am. J. Psychiatry* 152:833–42

Kendler KS, Kuhn J, Prescott CA. 2004. The interrelationship of neuroticism, sex, and stressful life events in the prediction of episodes of major depression. *Am. J. Psychiatry* 161:631–36

Kendler KS, Neale MC, Kessler R, Heath AC, Eaves LJ. 1993b. A twin study of recent life events and difficulties. *Arch. Gen. Psychiatry* 50:789–96

Kendler KS, Thornton LM, Gardner CO. 2000. Stressful life events and previous episodes in the etiology of major depression in women: an evaluation of the "kindling" hypothesis. *Am. J. Psychiatry* 157:1243–51

Kendler KS, Thornton LM, Gardner CO. 2001a. Genetic risk, number of previous depressive episodes, and stressful life events in predicting onset of major depression. *Am. J. Psychiatry* 158:582–86

Kendler KS, Thornton LM, Prescott CA. 2001b. Gender differences in the rates of exposure to stressful life events and sensitivity to their depressogenic effects. *Am. J. Psychiatry* 158:587–93

Kessler RC. 1997. The effects of stressful life events on depression. *Annu. Rev. Psychol.* 48:191–214

Kessler RC, Davis CG, Kendler KS. 1997. Childhood adversity and adult psychiatric disorder in the US National Comorbidity Survey. *Psychol. Med.* 27:1101–19

Kessler RC, Magee WJ. 1993. Childhood adversities and adult depression: basic patterns of association in a US national survey. *Psychol. Med.* 23:679–90

Kessler RC, Magee WJ. 1994. Childhood family violence and adult recurrent depression. *J. Health Soc. Behav.* 35:13–27

Ladd CO, Huot RL, Thrivikraman KV, Nemeroff CB, Meaney MJ, Plotsky PM. 2000. Long-term behavioral and neuroendocrine adaptations to adverse early experience. In *Progress in Brain Research*, ed. EA Mayer, CB Saper, pp. 81–103. New York: Elsevier

Lam DH, Green B, Power MJ, Checkley S. 1996. Dependency, matching adversities, length of survival and relapse in major depression. *J. Affect. Disord.* 37:81–90

Lee AL, Ogle WO, Sapolsky RM. 2002. Stress and depression: possible links to neuron death in the hippocampus. *Bipolar Disord.* 4:117–28

Lewinsohn PM, Allen NB, Seeley JR, Gotlib IH. 1999. First onset versus recurrence of depression: differential processes of psychosocial risk. *J. Abnorm. Psychol.* 108:483–89

Lewinsohn PM, Joiner TE Jr, Rohde P. 2001. Evaluation of cognitive diathesis-stress models in predicting major depressive disorder in adolescents. *J. Abnorm. Psychol.* 110:203–15

Maciejewski PK, Prigerson HG, Mazure CM. 2001. Sex differences in event-related risk for major depression. *Psychol. Med.* 31:593–604

Mazure CM. 1998. Life stressors as risk factors in depression. *Clin. Psychol. Sci. Pract.* 5:291–313

Mazure CM, Maciejewski PK, Jacobs SC, Bruce ML. 2002. Stressful life events interacting with cognitive/personality styles to

predict late-onset major depression. *Am. J. Geriatr. Psychiatry* 10:297–304

McGonagle KA, Kessler RC. 1990. Chronic stress, acute stress, and depressive symptoms. *Am. J. Community Psychol.* 18:681–706

McGuffin P, Katz R, Aldrich J, Bebbington PE. 1988. The Camberwell Collaborative Depression Study: II. Investigation of family members. *Br. J. Psychiatry* 152:766–74

McQuaid JR, Monroe SM, Roberts JE, Kupfer DJ, Frank E. 2000. A comparison of two life stress assessment approaches: prospective prediction of treatment outcome in recurrent depression. *J. Abnorm. Psychol.* 109:787–91

Meyer SE, Chrousos GP, Gold PW. 2001. Major depression and the stress system: a life span perspective. *Dev. Psychopathol.* 13:565–80

Monroe SM, Hadjiyannakis K. 2002. The social environment and depression: focusing on severe life stress. See Gotlib & Hammen 2002, pp. 314–40

Monroe SM, Simons AD. 1991. Diathesis-stress theories in the context of life stress research: implications for the depressive disorders. *Psychol. Bull.* 110:406–25

Nietzel MT, Harris MJ. 1990. Relationship of dependency and achievement/autonomy to depression. *Clin. Psychol. Rev.* 10:279–97

Nolen-Hoeksema S. 2002. Gender differences in depression. See Gotlib & Hammen 2002, pp. 492–509

Nolen-Hoeksema S, Girgus JS. 1994. The emergence of gender differences in depression during adolescence. *Psychol. Bull.* 115:424–43

Nolen-Hoeksema S, Larson J, Grayson C. 1999. Explaining the gender difference in depressive symptoms. *J. Personal. Soc. Psychol.* 77:1061–72

Ormel J, Oldehinkel AJ, Brilman EI. 2001. The interplay and etiological continuity of neuroticism, difficulties, and life events in the etiology of major and subsyndromal, first and recurrent depressive episodes in later life. *Am. J. Psychiatry* 158:885–91

Patton GC, Coffey C, Posterino M, Carlin JB, Bowes G. 2003. Life events and early onset depression: cause or consequence? *Psychol. Med.* 33:1203–10

Paykel ES. 1997. The interview for recent life events. *Psychol. Med.* 27:301–10

Paykel ES. 2003. Life events and affective disorders. *Acta Psychiatr. Scand.* 108:61–66

Paykel ES, Cooper Z. 1992. Life events and social stress. In *Handbook of Affective Disorders*, ed. ES Paykel, pp. 149–70. New York: Guilford

Plotsky PM, Owens MJ, Nemeroff CB. 1998. Psychoneuroendocrinology of depression: hypothalamic-pituitary-adrenal axis. *Psychiatr. Clin. N. Am.* 21:293–307

Post RM. 1992. Transduction of psychosocial stress into the neurobiology of recurrent affective disorder. *Am. J. Psychiatry* 149:999–1010

Post RM, Rubinow DR, Ballenger JC. 1984. Conditioning, sensitization, and kindling: implications for the course of affective illness. In *Neurobiology of Mood Disorders*, ed. RM Post, JC Ballenger, pp. 432–56. Baltimore, MD: Williams & Wilkins

Potthoff JG, Holahan CJ, Joiner TE. 1995. Reassurance seeking, stress generation, and depressive symptoms: an integrative model. *J. Personal. Soc. Psychol.* 68:664–70

Poulton RG, Andrews G. 1992. Personality as a cause of adverse life events. *Acta Psychiatr. Scand.* 85:35–38

Rijsdijk FV, Sham PC, Sterne A, Purcell S, McGuffin P, et al. 2001. Life events and depression in a community sample of siblings. *Psychol. Med.* 31:401–10

Riso LP, Miyatake RK, Thase ME. 2002. The search for determinants of chronic depression: a review of six factors. *J. Affect. Disord.* 70:103–16

Robins CJ. 1990. Congruence of personality and life events in depression. *J. Abnorm. Psychol.* 99:393–97

Rojo-Moreno L, Livianos-Aldana L, Cervera-Martinez G, Dominquez-Carabantes JA, Reig-Cerbrian MJ. 2002. The role of stress in the onset of depressive disorders: a controlled

study in a Spanish clinical sample. *Soc. Psychiatry Psychiatr. Epidemiol.* 37:592–98

Rudolph KD. 2002. Gender differences in emotional responses to interpersonal stress during adolescence. *J. Adolesc. Health* 30:3–13

Rudolph KD, Hammen C. 1999. Age and gender as determinants of stress exposure, generation, and reactions in youngsters: a transactional perspective. *Child Dev.* 70:660–77

Rudolph KD, Hammen C, Burge D, Lindberg N, Herzberg D, Daley SE. 2000. Toward an interpersonal life-stress model of depression: the developmental context of stress generation. *Dev. Psychopathol.* 12:215–34

Rutter M. 1986. Meyerian psychobiology, personality development, and the role of life experiences. *Am. J. Psychiatry* 143:1077–87

Schinka J, Busch R, Robichaux-Keene N. 2004. A meta-analysis of the association between the serotonin transporter gene polymorphism (5-HTTLPR) and trait anxiety. *Mol. Psychiatry* 9:197–202

Segal ZV, Shaw BF, Vella DD, Katz R. 1992. Cognitive and life stress predictors of relapse in remitted unipolar depressed patients: test of the congruency hypothesis. *J. Abnorm. Psychol.* 101:26–36

Segrin C. 2001. Social skills and negative life events: testing the deficit stress generation hypothesis. *Curr. Psychol. Dev. Learn. Personal. Soc.* 20:19–35

Sen S, Villafuerte S, Nesse R, Stoltenberg SF, Hopcian J, et al. 2004. Serotonin transporter and GABA(A) alpha 6 receptor variants are associated with neuroticism. *Biol. Psychiatry* 55:244–49

Shrout PE, Link BG, Dohrenwend BP, Skodol AE, Stueve A, Mirotznik J. 1989. Characterizing life events as risk factors for depression: the role of fateful loss events. *J. Abnorm. Psychol.* 98:460–67

Simons AD, Angell KL, Monroe SM, Thase ME. 1993. Cognition and life stress in depression: cognitive factors and the definition, rating, and generation of negative life events. *J. Abnorm. Psychol.* 102:584–91

Spangler DL, Simons AD, Monroe SM, Thase ME. 1996. Gender differences in cognitive diathesis-stress domain match: implications for differential pathways to depression. *J. Abnorm. Psychol.* 105:653–57

Strickland PL, Deakin JFW, Percival C, Dixon J, Gater RA, Goldberg DP. 2002. Bio-social origins of depression in the community: interactions between social adversity, cortisol and serotonin neurotransmission. *Br. J. Psychiatry* 180:168–73

Swindle RW, Cronkite RC, Moos RH. 1989. Life stressors, social resources, coping, and the 4-year course of unipolar depression. *J. Abnorm. Psychol.* 98:468–77

Tennant C. 2002. Life events, stress and depression: a review of the findings. *Aust. NZ J. Psychiatry* 36:173–82

Thase M, Jindal R, Howland R. 2002. Biological aspects of depression. See Gotlib & Hammen 2002, pp. 192–218

van Os J, Jones PB. 1999. Early risk factors and adult person-environment relationships in affective disorder. *Psychol. Med.* 29:1055–67

Weiss EL, Longhurst JG, Mazure CM. 1999. Childhood sexual abuse as a risk factor for depression in women: psychosocial and neurobiological correlates. *Am. J. Psychiatry* 156:816–28

Whiffen VE, Clark SE. 1997. Does victimization account for sex differences in depressive symptoms? *Br. J. Clin. Psychol.* 36:185–93

Young EA, Lopez JF, Murphy-Weinberg V, Watson SJ, Akil H. 2000. Hormonal evidence for altered responsiveness to social stress in major depression. *Neuropsychopharmacology* 23:411–18

Zimmerman M, Coryell W, Pfohl B. 1986. Validity of familial subtypes of primary unipolar depression: clinical, demographic, and psychosocial correlates. *Arch. Gen. Psychiatry* 43:1090–96

Zuroff DC, Mongrain M, Santor DA. 2004. Conceptualizing and measuring personality vulnerability to depression: comment on Coyne and Whiffen 1995. *Psychol. Bull.* 130:489–511

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