

Oxford Handbooks Online

Stress in Depression

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The Oxford Handbook of Stress and Mental Health

Edited by Kate Harkness and Elizabeth P. Hayden

Subject: Psychology, Clinical Psychology Online Publication Date: Jan 2019

DOI: 10.1093/oxfordhb/9780190681777.013.5

Abstract and Keywords

That life stress precipitates depression is one of the most replicated findings in psychiatric research, but prior to Brown and Harris's seminal contributions, insufficiently rigorous methods led to underestimates of the effects of stress and threatened the field. This chapter provides a methodological and historical overview, followed by a review of evidence that recent stress predicts depression across the life span. It also examines demographic vulnerability factors and research on early adversity and depression, closing with future directions. Two themes manifest throughout. First, stress assessment that uses investigator-rated severity, accounts for severity, establishes temporal precedence, and isolates the few months prior to depression onset remains critical to progress. Second, identifying the most potent forms of stress for depression is a key question that will facilitate both preventive/intervention efforts and more powerful tests in mechanistic research. Although evidence points to interpersonal forms of stress, few studies provide the necessary direct tests.

Keywords: life stress, early adversity, stressful life events, chronic stress, major difficulties, adults, adolescents, children, depression

Few findings in psychiatric research are as consistent and well documented as the conclusion that validly assessed life stress causes unipolar major depressive disorder. And yet, this seemingly well-explored topic persists in captivating researchers, mental health practitioners, and lay people alike. The topic's continued draw likely reflects two truths. First, depression is a paramount public health concern—among the most common and costly of illnesses (Ferrari et al., 2013; Greenberg et al., 2003). Thus, understanding the mechanisms by which it emerges and endures is very likely to lead to interventions that reduce both suffering and economic cost to society. Second, evidence from behavioral genetic studies indicates that environmental factors unique to the individual, perhaps chiefly life stress, contribute a majority of the variance in risk for depression (a meta-

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analytic point estimate of 63%; Sullivan, Neale, & Kendler, 2000). Thus, efforts to understand the stress-depression link are likely to be valuable to society.

What is critical to appreciate about the contemporary understanding of the robust, causal association between life stress and depression is that, for a time, this conclusion was very much in doubt—and the reasons for the reversal of this opinion over time are relevant to current research. Four critical methodological factors led to stronger, more persuasive data: using contextual investigator-rated assessment interviews, ascertaining the temporal precedence of stressors before depression onsets, accounting for stressor severity in one of several ways, and isolating a relatively brief window of time prior to disorder onsets. We will argue that for stress and depression research to advance in an age of brief measures and “big data,” it will not only be necessary to continue to adhere to those four methodological advances but also to hone in on which forms of stress are most potent with greater methodological care.

In this chapter, we examine evidence for the relationship between stress and depression. Following key definitions of stress, we first provide a brief introduction to methodological issues critical to evaluating the stress and depression literature, which we elaborate on as relevant throughout the chapter. We then divide our review by the timing of stress—examining recent stress for the majority of the chapter, followed by early life adversity in a shorter section. Within our review of recent stress, following a historical overview, we structure our review by developmental period in reverse chronological order from adulthood to adolescence to childhood, with more discussion devoted to findings in adults and about stressful life events, reflecting the relative balance of the literature. Throughout the chapter, we consider what forms of stress are most potent and the methodological reasons that existing work struggles to definitively answer this question. We conclude the discussion of recent stress by highlighting demographic differences in stress exposure and sensitivity. Although models of the action of stress on depression emphasize the role of pre-existing risk factors or diatheses, these are reviewed in other chapters on cognitive (see Hankin & Schweizer, this volume), personality (see Olino, Wojcieszak, & Mennies, this volume), and genetic (see Uher, this volume) vulnerabilities. In addition to highlighting future directions in review subsections throughout the chapter, we close with overarching future directions and emphasize the importance of delineating the most potent forms of stress in the onset of depression.

Key Definitions

Researchers have focused primarily on three broad forms of stress in the pathway to depression—stressful life events, chronic stress, and early adversity (for examples of each, refer to Table 1). Stressful life events refer to acute occurrences that confer relatively long-term (> 1 week) negative impact or threat on any aspect of the individual’s life; we describe various dimensions of events later. Although chronic stress, also known as chronic difficulties, has been operationalized in different ways, it consistently captures more long-standing challenges than do acute events. By contrast, early adversity—which often encompasses childhood and adolescent adversity—typically represents an amalgam of events and chronic stress rather than distinguishing between them. It is instead defined by the early developmental stage (i.e., prior to adulthood) in which it occurred. Depending on the measure used in assessment, early adversity may capture maltreatment by a caregiver as well as adversity that is out of the control of the caregiver (e.g., death of a parent).

Table 1 Examples of Types of Life Stress	
Form of Stress	Example(s)
Major event	Although severity is assigned by rating teams based on the full context of events, the sudden, unexpected death of a very close loved one such as a partner, best friend, or child would typically be rated as a major event.
Minor event	Although severity depends upon the full context of the event, an argument among a group of friends that lasts for 5 days but lacks long-term impacts (> 1 week) to the friend group and other aggravating features would often be rated as a minor event.
Interpersonal event	Loss of a loved one; romantic breakup; argument with friend, partner, or family member; separation from a close other.
Noninterpersonal event	Failing a course, job loss, acute illness or injury to oneself, acute financial problems
Dependent event	Argument with a friend, partner, or family member, failing a course, a car accident where one is at fault

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Independent event	Being the victim of a crime, death of a loved one, being diagnosed with an illness
Interpersonal chronic stress or major difficulty	Examples vary across assessment tools, but an elevation in LSI chronic stress consistent with a LEDS major difficulty would be frequent conflict and lack of emotional support for over 2 years in a romantic relationship
Noninterpersonal chronic stress or difficulty	Examples vary across assessment tools, but an elevation in LSI chronic stress consistent with an LEDS major difficulty would be employment for 2 years or more
Early adversity, including maltreatment	For example, any of the following occurring to an individual below the age of 18; often divided into childhood adversity and adolescent adversity: • Separation or loss: a parent leaving the family or being imprisoned • Physical neglect: inappropriate, insufficient levels of supervision for the developmental stage (being left alone overnight at age 5) • Emotional abuse: name-calling, blaming the minor for things for which he or she is not responsible; • Sexual abuse: molestation, incest, being shown pornographic materials • Physical abuse: hitting, physical punishments, being locked out of the home in the cold as punishment

Note: Event types are not mutually exclusive; that is, an event can be major, interpersonal, and dependent, for example. The examples provided are intended to be illustrative rather than comprehensive.

Methodological Considerations in Life Stress and Depression Research

Several methodological points inform our approach in this chapter and merit brief discussion prior to the literature review. First, here we use the term “stress” to refer to objective, negative life circumstances (such as the forms defined earlier), based on a conceptualization of stress as the environmental pressure exerted on an individual (e.g.,

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Dohrenwend & Dohrenwend, 1969). This conceptualization contrasts with one in which stress captures the individual's physiological or emotional *response* to that environmental pressure or his or her *perception* of stress (referred to as "biologic stress;" e.g., Selye, 2013). This distinction is critical for reasons we describe later in the historical overview of stressful event methodology. Second, our emphasis on objective stress necessitates a focus on forms of assessment that ensure objective stress, and not perceptions or responses to stress, are captured. Thus, we have primarily cited evidence utilizing objective interview-based measures in which investigators make judgments based on the full context of events—not self-report questionnaires or checklists, due to known validity problems (e.g., Harkness & Monroe, 2016; McQuaid et al., 1992). In cases where we felt it was necessary to mention questionnaire-based studies, we have noted the methodological approach for readers.

Third, although there is a well-characterized *bidirectional* relationship between objective stress and depression (see Hammen, this volume), here we focus on evidence that stress causally precipitates depression. The critical methodological ingredient for ensuring potential causality is establishing *temporal precedence* of stress before depression. Temporal precedence refers to stressful circumstances occurring prior to depression onset (e.g., job termination leading to depression onset), and not vice versa (e.g., difficulty getting out of bed when depressed, causing tardiness to work, leading to job termination). Because depression is known to generate stress for individuals, to prevent overestimating the causal impact of stress on depression, it is critical to use only instances in which the stressor occurred first. The need for temporal precedence requires that studies examine stress and depressive episodes longitudinally, rather than examining cross-sectional relationships between recent stress and current depression. Even longitudinal research on stress, however, is not usually truly prospective (i.e., assessing stress at one timepoint and depression at another). In most cases, recent stress and depression are retrospectively assessed simultaneously, and careful dating is used to establish temporal precedence. Cross-sectional research that cannot establish temporal precedence is less authoritative than longitudinal research additionally because, in community samples, this approach is likely to overlook episodes triggered by stress in the recent past and thereby underestimate the effects of stress. We have therefore de-emphasized work that relies on cross-sectional analyses and have pointed to this methods choice when we did choose to cite such work.

Recent Stress Impacts Depression in Adults

Historical Overview

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A large body of research has established that recent stress precipitates depression during adulthood; we begin by providing some historical context, which is vital for understanding how life stress research should proceed.

Holmes and Rahe's Problematic Questionnaire Measures

Some of the first and most widely cited systematic evidence to link life experiences to the onset of several types of physical illness (Rahe, Meyer, Smith, Kjaer, & Holmes, 1964) stimulated later work on stress and depression and used the Schedule of Recent Events (SRE; Hawkins, Davies, & Holmes, 1957). As reviewed by Rahe (1978), the SRE was developed in the 1950s and used a checklist format to inquire whether and when 42 events had occurred within the past 10 years. It was later expanded to add 13 experiences and was renamed as the Recent Life Changes Questionnaire (Rahe, 1975). Similar work attempting to account not only for occurrence of events but also their relative severity relied on the Social Readjustment Rating Scale (SRRS), which used severity "weights" derived from studies using the Social Readjustment Rating Questionnaire (SRRQ; Holmes & Rahe, 1967). To develop the SRRS, Holmes and Rahe selected healthy participants (to prevent bias introduced by ill individuals) and surveyed them using the SRRQ about how intense and lengthy they felt that adjustment to 43 experiences would be for the average person—ignoring the desirability of each experience. These resulted in average weights assigned to each type of experience (e.g., death of a spouse = 100, marriage = 50, beginning or ending school = 26, vacation = 13). In the SRRS, these average weights were multiplied by event frequency in the past year to derive a total score. The extension of these questionnaire-based approaches from physical illnesses to mood disturbances followed in epidemiological samples that relied on cross-sectional self-reports and utilized correlational analyses. For example, Rahe (1974) applied this approach in two samples of thousands of US and Norwegian sailors who provided questionnaire reports of depression symptoms and their changes in life circumstances, resulting in correlations of $r = .22$ and $.36$, respectively (also see Myers, Lindenthal, & Pepper, 1971; Rahe, 1979).

The many methodological flaws of this approach and its resulting small effect sizes, however, ultimately led to doubt about the effects of events on illness. For example, in a review of studies relying on Holmes and Rahe's SRE, Tausig (1982, p. 52) later concluded that "attempts to observe stress have generally yielded low to modest estimates of the contribution of stressful events to the appearance of some order of disturbance," including depression. Although these problems led one reviewer to conclude that the checklist approach had been abandoned (Mazure, 1998), it has since resurged in at least one research area seeking rapid, inexpensive measures of stress (for a discussion, see Monroe & Reid, 2008).

Brown and Harris Introduce Contextual Threat Methods

Prompted by this emerging pessimistic view of the effect of events and by the methodological flaws inherent in checklist and average-weight assessment approaches, Brown and Harris and colleagues published seminal contributions that have

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fundamentally shaped the conceptualization and measurement of life stress in psychopathology. In an often overlooked commentary, Brown, Sklair, Harris, and Birley (1973) first outlined three critical and timeless sources of potential bias in the assessment of life events that point to the importance of interviewer ratings of stressor context and to the sheer implausibility of stressor checklist validity. First, they point to “effort after meaning,” the attempt to provide a post hoc explanation for an undesired outcome, citing evidence that mothers of babies with certain serious birth defects report more negative events during pregnancy, whereas later work showed that chromosomal abnormalities were to blame. Second, they note that individuals experiencing a depression onset may experience events as more severe than they ordinarily would—confounding the measure of stress exposure with vulnerability, perceived stress, and stress *response*. The implication of these first two potential sources of bias is that the investigator should determine whether to include a reported event and what severity rating to assign it.

Third, they identified that it was critical to develop conventions for what qualified as an event (a minimum threshold) across interviewers to apply common standards. To address these issues, the authors introduced the important methodological advancement of an investigator-rated severity scale. The interviewer (though in these same researchers’ later approaches, blind raters) judged the level of “threat or difficulty implied by the event once the more immediate effects were over ... about one week after its occurrence” (G. Brown et al., 1973, p. 77) for a typical person in all the same circumstances, taking no account of the participant’s report of severity, from 1 to 4 (none, little, moderate, or marked).

Soon after, Brown and Harris (1978) debuted their watershed *Social Origins of Depression* text describing the Camberwell studies of life stress and depression in working-class British women ages 1–65, which formed the basis for the Life Events and Difficulties Schedule (LEDS; Bifulco et al., 1989). Participants for the primary analyses were 114 psychiatric inpatients and outpatients (73 and 41, respectively) with a primary depression diagnosis and no comorbid alcohol dependence or psychotic disorder, a comparison group of 382 women from the same community without psychiatric diagnoses, plus 37 community women discovered to have had past-year depressive episode onsets on interview, but who had not sought treatment. In this study, unlike their previous one, interviewers collected detailed information about each event’s context from the participant and presented this information to a rating team blind to the participant’s diagnosis and emotional response to the event.

The primary conclusions of this seminal study were that, from an array of 28 event characteristics examined, *long-term* contextual threat (i.e., threat 1 week after the event occurred) appeared most critical in precipitating an episode of depression. “Severe” events (those with moderate to marked long-term contextual threat level—the top 2 points of the 4-point scale—which we also refer to as “major events” throughout) were present among 61% of patients and 68% of women with untreated onsets, versus 20% of controls in the 38 weeks prior to a depression onset among patients compared to the same period prior to interview among controls. Similarly, Brown and Harris investigated

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the relative frequency of all “difficulties” (more long-standing challenges lasting at least 4 weeks and not arising due to an event), blindly rated on a 6-point severity scale. They reported that only those difficulties of 2 years or longer in duration, rated in the highest 3 points of the scale, and not involving health problems—which they then coined *major difficulties*—were linked with depression. Specifically, 47% of patients and 49% of women with untreated onsets, versus 17% of controls, experienced at least one major difficulty in the 38 weeks prior to illness onset or interview.

Additional Early Findings for Recent Stress

These findings implicating severe events and major difficulties echoed Brown and Harris’s earlier work predicting “psychiatric disturbances” broadly—much of which was depression—in 114 adult women patients seeking treatment and 220 randomly selected community women (G. Brown, Bhrolchain, & Harris, 1975). Findings were also consistent with evidence of their contemporaries who used similar interview-based measures, evaluated severity, and established temporal precedence. For example, severe recent events were more common prior to depression onset than in a comparable period of time in controls (Paykel, 1976) and severe recent events predicted postpartum depression among women assessed 6 weeks after delivery (Paykel, Emms, Fletcher, & Rassaby, 1980). Their 1978 findings were also mostly consistent with work that emerged soon after their report, which addressed any concern about the treatment-seeking nature of the original sample. Brown and Harris (1989) summarized the findings of 10 samples of women from the general population studied using the LEDS published between 1978 and 1986. This revealed that 84% of women (218 of 261) with a major depressive episode onset experienced at least one severe event or major difficulty prior to onset (ranging from 3 months to 1 year) compared to only 32% of nondepressed control women (558 of 1,745) who experienced either form of stress in a comparable timeframe (G. Brown & Harris, 1989). The percentage of affected individuals experiencing a severe event ranged from 42% to 93% (68% in aggregate), while the percentage experiencing a major difficulty ranged from 15% to 55% (38% in aggregate), leading Brown and Harris to conclude that the results for chronic stress were “somewhat less consistent than those for events” (p. 58).

Thus, the work of Brown and Harris and their like-minded contemporaries provided evidence for the value of contextual investigator-rated assessment of life stress and set the standard for four subsequent decades of stress and depression research, which we now review. In the review of recent stress in adults, we first discuss stressful life events, second chronic stress, and last, demographic predictors of stress exposure and sensitivity.

Stressful Life Events

To probe the relationship between stressful life events and depression, we examine evidence for (1) the role of event severity, (2) whether multiple events increase risk, (3)

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duration of event potency, (4) which event types appear to be the most important, and (5) the extent to which events are causally related to depression.

Severity of Events

One of the most consistent findings within event and depression research is that major severity events significantly increase risk for depression onsets, while lesser severity minor events generally do not (see Table 1 for event examples). Evidence for this emerged from some of the earliest interview-based studies (G. Brown & Harris, 1978; Paykel et al., 1980; Shrout et al., 1989; Surtees et al., 1986) as well as in the years that followed (e.g., Kendler, Karkowski, & Prescott, 1998; Vrshek-Schallhorn et al., 2015). However, the early literature focused so rapidly on severe events that, in many cases, minor event effect sizes are not included (e.g., Costello, 1982), and others have summed the severity scores of all events (Hammen, Kim, Eberhart, & Brennan, 2009). Despite the implication that severity is dichotomous, when examined in one very large study (albeit one in which interviewers and not blind raters assigned severity), the best-fitting models indicated a linear dimensional effect of severity (Kendler et al., 1998).

When minor events uncharacteristically do appear to precipitate depression, stress sensitization by prior depression may have increased the person's vulnerability (for a more detailed review, see Stroud, this volume), based on Post's (1992) "kindling" hypothesis that recurrences of depression occur in response to progressively less severe events. In one 5-year longitudinal study of older adolescent women, interview-assessed minor events significantly grew in their impact (i.e., risk of depression onset given the presence of a recent event) for recurrences compared to first onsets, whereas major events did not significantly change in impact between first onsets versus recurrences, remaining a significant predictor of both (Stroud, Davila, Hammen, & Vrshek-Schallhorn, 2011). This finding expanded on other work showing associations of minor events with recurrences of depression (Lenze, Cyranowski, Thompson, Anderson, & Frank, 2008; Monroe, Roberts, Kupfer, & Frank, 1996; Monroe et al., 2006; Ormel, Oldehinkel, & Brilman, 2001; Rudolph & Flynn, 2007).

Number of Events

Next, a number of studies—but not all—support that multiple events increase risk for depression onset beyond the effect of a single event. In an analysis combining all severities of interview-assessed events, an increasing number of events robustly increased risk for depression onset, with risk following an exponential growth pattern (Kendler et al., 1998). Importantly, however, when investigators have not accounted for events' severity as in this case, an alternative explanation is that as the number of events increased, so did the probability of experiencing one major event (which then increased the likelihood for depression). Yet two other studies did account for event severity and indicate that multiple events increase risk regardless of severity. First, statistical models examining how the impact of interview-assessed events declines as time passes (i.e., decay models) better predicted depression onset when *all* events experienced were included in an additive fashion, rather than when models were simplified to represent the

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presence of at least one severe event (Surtees, 1989). This suggested that multiple events behaved in a cumulative and dimensional fashion to raise risk, such that major events increased risk more and for longer duration than did minor ones, which had a very short-lived impact. Second, among a small sample ($N = 52$) of people with highly recurrent depression (median of 4 lifetime episodes) whose most recent episode was preceded by at least one severe interview-assessed event in the prior 6 months, those who experienced at least one additional event—whether severe or minor—had an episode onset sooner following the severe event than those who did not (Frank et al., 1996). Contrasting other evidence, in the Camberwell Studies, experiencing multiple severe events was only associated with increased risk for depression when the severe events were *unrelated* to each other—and even then, the increase in risk due to having a second or third event was relatively small (G. Brown & Harris, 1978). Thus, despite some inconsistency in these findings, the balance of evidence appears to indicate that multiple events increase risk for depression onset.

Duration of Stressor Impact

Several types of evidence suggest that the effects of stressful experiences for increased depression risk fade relatively quickly after stress exposure ends, and that using an appropriate timeframe in analyses is critical to maximizing effects. Several studies have used fine-grained, month-to-month approaches, but one twin study with repeated assessments used a latent variable approach in a sample of women in middle adulthood to first isolate the unique environmental contribution to depression risk, and second to tease apart the relative contribution of the past-year environment versus that prior. Of the unique environmental variance, past-year factors accounted for 70%, while experiences occurring prior to the past year accounted for only 13% and diagnostic error accounted for 17% (Kendler & Gardner, 2017). This supports a relatively larger contribution of past-year stressors than earlier life stressors, at least in this sample's age range.

Converging evidence using a more fine-grained approach also suggests that stressful life events confer significant risk for depression for a relatively brief amount of time not longer than several months. Investigations using interview methods showed that (1) events precipitated depression most often within 3 weeks and almost always within 9 weeks of the event (G. Brown & Harris, 1978), (2) events significantly predicted depression for 1 month, but not later (Kendler et al., 1995), and (3) decay models approximating the declining impact of events over time indicated events are significantly impactful for depression onset no longer than 13 weeks (Surtees & Wainwright, 1999). In one study that suggested somewhat greater heterogeneity in duration of event impact on risk, this appears to be due to combining acute events with more long-standing problems similar to Brown and Harris's (1978) chronic difficulties (Kendler et al., 1998). In sum, most evidence indicates that stressful events exert their risk-increasing effects for depression onset within the first month and not beyond 3 months after event occurrence. Based on this evidence, most recent research on stressful events examines the past 1 to 3

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months to predict episode onsets; using longer periods of time dilutes estimates of the effects of events for depression.

Event Type

Research has examined several characteristics of stress thought to contribute to potency in hopes of elucidating how stress precipitates depression; the two earliest identified event characteristics implicated were independence, which we discuss first, and loss, which we discuss second. A major methodological weakness of most of this research is that investigators most often “compare” the effects of different types of events by testing whether each, separately, is a statistically significant predictor of depression and concluding that the significant predictor is more important than the nonsignificant one. We highlight rare examples when investigators test the difference between effect sizes—a step needed to support the inference that one form of stress is more potent than another.

Event Dependence-Independence

Terminology related to independence differs somewhat across methodologies, with one capturing *illness* independence and other independence from the participant’s *behavior*. This distinction was initially of interest to researchers because it was reasoned that a link between independent events and depression onsets would strengthen confidence about the causal role of stress in illness onset (G. Brown & Harris, 1978). Brown and Harris (1978) thus classified events as “independent” (chance or fateful events such as an employer closing down that could not have been evoked by illness), “possibly independent” (events such as marital separation, when it appeared that illness followed rather than preceded the event, but the event was not a chance or fateful occurrence), and “illness-related” events that clearly occurred after depressive onset. Brown and Harris (1978) excluded this latter category of events from analyses due to their lack of temporal precedence. They reasoned a link between independent events and illness would rule out the possibility that subclinical symptoms caused events and then grew into clinically significant illness manifestations (pp. 73–74). In a different life events interview loosely inspired by the LEDS, however, Hammen categorized events as “probably independent of the subject, probably dependent on the subject, or ambiguous (possibly both dependent and independent)” (emphasis added; Hammen, Marks, Mayol, & DeMayo, 1985, p. 312). Importantly, in research that has followed using Hammen’s approach, ambiguous events (including many interpersonal events such as marital separation, defined as “possibly independent” by Brown and Harris) have been classified with *dependent* events because they are thought to be at least partly caused by the individual’s behavior or characteristics. This distinction later took on new meaning as investigators began to seek potent events to maximize the stress-depression effect size (Surtees et al., 1986).

It is evident from the research that followed that independent events (at least major ones) usually predict depression onset, but the case that either independent or dependent events are more potent is flawed. A strong theoretical case for either is lacking in the literature, and overall, evidence for dependence and independence has been equivocal:

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Studies that initially appear to implicate either independent or dependent events rarely in fact do so when examined more closely. Two initially appear to implicate independent events as more potent. First, in a community sample of 449 women including 38 depression onsets, events which were “possibly independent”—those that might or might not have been caused partly by the woman’s behavior—had a “particularly strong” association with depression (as opposed to fully independent events), but the authors neither directly tested whether these events were more potent, nor delineated which events were dependent on the participant’s behavior (Costello, 1982). Second, in a sample of 96 depressed patients and 404 nondepressed controls, although interview-assessed severe independent events discriminated patients from controls, when examined separately, it was event severity and not event independence that discriminated depressed patients from controls (Shrout et al., 1989).

Conversely, two studies initially appear to implicate dependent events as more potent. First, in a comparison of 35 women with recent onsets of depression with 485 nondepressed women, both recent event severity and event dependence alone significantly discriminated between the two groups (Surtees et al., 1986), but our confidence in these findings is reduced because of the small sample of depressed women, coupled with the possibility that dependent events may have also been more severe. Second, in a large twin study sample, direct tests showed dependent events to be significantly more likely to precipitate depression than independent events (Kendler, Karkowski, & Prescott, 1999). However, this test was conducted for an aim other than identifying the most potent type of event, and likely for this reason, other potentially confounding event dimensions, including severity and interpersonal status (defined later), were not accounted for. Consistent with this explanation, in two samples of emerging adults, once interview-rated event severity and interpersonal status were accounted for, dependence did not further refine which stressors uniquely predicted depression onsets (Vrshek-Schallhorn et al., 2015). Taken together, the evidence reflects that event independence versus dependence is not critical for determining the likelihood of precipitating depression on average, particularly once other dimensions are accounted for.

Loss and Related Dimensions

Loss was defined broadly by Brown and Harris (1978) to include real or threatened separations from loved ones, including deaths, negative revelations about a close other (i.e., loss of one’s positive conceptualization of the relationship), life-threatening illness of a close other, real or threatened material loss or disappointment, real or threatened forced change in housing, and a miscellaneous loss category including job elimination. Brown and Harris (1978) noted that in the Camberwell Studies, upward of 70% of severe events regardless of the study group (patients, community onsets, or nondepressed controls) involved some element of loss. They interpreted this to mean that loss is critical to the etiology of depression, but provided little inferential statistical support for this assertion. In this same work, they suggested that danger (severe threat without the element of loss) was linked with mixed depression and anxiety manifestations, but again

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based this conclusion on their impressions of the data. Subsequent work, however, statistically supported a role for loss in depression and a role for danger in anxiety cases. Among 164 patients with depression, anxiety, or both, plus healthy controls, recent interview-assessed major loss events were more common prior to depression onset than they were in controls in a comparable timeframe. By contrast, recent major danger events were reported more commonly by anxiety patients than controls, and both forms of major events were implicated in combined depression and anxiety onsets (Finlay-Jones & Brown, 1981). Critically, however, this did not establish that either type of event was more potent than other events.

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Potentially Critical Aspects of Loss: Tests of Humiliation, Entrapment, and Bereavement

Brown's research group later advanced the idea that certain kinds of loss—those with high potential for evoking feelings of humiliation or of being trapped (“entrapment”)—may be the most potent. In 353 community mothers of children completing LEDS interviews spanning 2 years, severe humiliation and entrapment events (a combined category) preceded depression onsets significantly more often than did losses without those elements. This difference was demonstrated by a chi-squared test followed by orthogonal contrast post hoc tests. In addition, though not predicted, bereavement events were also significantly more potent than nondeath losses (G. Brown, Harris, & Hepworth, 1995). In a replication, among 172 randomly selected suburban Zimbabwean women, severe humiliation, entrapment, or bereavement events in the LEDS were significantly more likely to precede depression than were other severe loss or danger events (Broadhead & Abas, 1998).

These initial tests of the primacy of humiliation and entrapment had three important limitations. First, they did not permit generalizations to men. Second, humiliation and entrapment were included in a single category for inferential statistics on event potency, which begged the question of whether both types were in fact similarly potent. Third, the hierarchical and dichotomous rating approach applied only evaluated whether events were losses or danger events if they were not first rated as humiliations or entrapments. This approach prohibited tests of multiple event attributes simultaneously and obscured that many humiliations and entrapments were also losses. A third study addressed each of these issues.

Kendler et al. (2003) used investigator ratings of dimensional likelihood of humiliation, loss, danger, and entrapment for all severe events of 7,322 male and female adult members of twin pairs. In separate analyses, the loss and humiliation dimensions were significantly related to onsets of pure depression or depression combined with generalized anxiety within the month following event occurrence. Danger and entrapment were not significantly related at any point to pure depression, although each predicted the combined depression and anxiety syndrome a month after the event. Further, the effect of these dimensions did not vary by gender in interaction tests, extending results for humiliation and loss to males. Importantly, in a model containing both humiliation and loss dimensions to account for their correlation, both continued to significantly and uniquely predict depression onsets (Kendler, Hettema, Butera, Gardner, & Prescott, 2003). However, there were no explicit tests of the difference of effect sizes of these types of events, so although the loss dimension had a descriptively larger effect size than humiliation, it cannot be said that the loss dimension is more potent than humiliation. Similarly, bereavement was not assessed as its own dimension, and effect sizes for bereavement losses were similar in magnitude (with overlapping confidence intervals) to nonbereavement losses.

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What can be concluded about humiliation, entrapment, danger, loss, and bereavement? There is clearly not good evidence that danger alone is particularly important for depression, and entrapment was either combined with humiliation in tests or was not a critical predictor when tested alone, suggesting this evidence is weak. Loss, humiliation, and to a lesser extent bereavement, however, have stronger, if imperfect, evidence bases.

Recent Investigations Examine Targeted Rejection and Broad Interpersonal Status

More recently, loss, humiliation, and bereavement have received less attention, as investigators have examined related but different dimensions. One such dimension, targeted rejection, refers to an intentional severing of a social relationship with an individual. For example, a one-sided romantic breakup represents a targeted rejection of one person, whereas a mutually agreed-upon romantic breakup does not. Among people with a recent depressive episode onset following a stressful event, those with a targeted rejection event became depressed an average of 30.4 days after the event, significantly faster than those who experienced a different type of event, who had onsets an average of 107.5 days later, suggesting that targeted rejection might be particularly potent (Slavich, Thornton, Torres, Monroe, & Gotlib, 2009). A second such dimension examines a theme common to loss, humiliation, bereavement, and targeted rejection: All are interpersonal in nature.

Beyond evidence from the dimensions of loss, humiliation, and bereavement, theory has implicated the broader dimension of interpersonal stress (that which primarily impacts the quality or quantity of relationships with other people) as central to depression risk (e.g., Joiner & Timmons, 2009; Whisman, 2001). Providing evidence for interpersonal stress, one study using two independent samples of emerging adults examined multiple forms of stress simultaneously in a single model per sample to account for correlations among forms of stress. Interpersonal forms of stress (both major events and chronic stress) consistently predicted depressive episode onset over and above other forms of stress in the model (i.e., statistically unique prediction). By contrast, noninterpersonal major events emerged as statistically unique predictors in very limited instances (Vrshek-Schallhorn et al., 2015). Further, in this study, both interpersonal chronic and episodic stress contributed significantly greater unique variance to depression onset than did their noninterpersonal counterparts—a rare direct test of the difference in magnitude of effect size. Taken together with prior evidence for the potential importance of humiliation, loss, and bereavement, all of which have strongly interpersonal themes, there is collectively a relatively strong body of evidence for the importance of various forms of interpersonal stress in depression.

Future Directions for Acute Life Events and Depression Research

In the preceding section, we have reviewed evidence that (1) event severity is critical in the stress-depression pathway, (2) multiple events increase depression risk beyond the occurrence of a single event, (3) the effects of stressful events on increased depression risk fade within 3 months, and (4) there is good evidence that events with interpersonal elements (including humiliations, losses, bereavements, and targeted rejections) are

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particularly potent for depression, whereas there is not good evidence that the dependence-independence distinction matters much. Extant research, however, has not yet considered a number of potentially important questions.

First, when evaluating whether the occurrence of multiple events heightens risk for depression compared to single event occurrence, the extant studies do not account for event independence versus dependence. Although we concluded that this distinction is not critical for event potency, the patterns of event clusters might be meaningful in another way. Successive dependent events might indicate that declining functioning and stress generation were involved in a downward spiral following an initial event, rather than supporting an exclusively causal pathway of multiple events to depression—and this would have meaningful implications for depression prevention. Thus, in the future, studies should characterize the independence of multiple events occurring prior to depression onset.

Second, the use of retrospective measures of stressful events has marked value for some questions. For mechanistic questions, however, retrospective measures preclude “real-time” collection of multimodal variables during the peak risk window following an event. Existing efforts to examine unfolding stress utilize individuals who have recently received life-altering medical diagnoses (e.g., stroke; Ramasubbu, Tobias, Buchan, & Bech-Hansen, 2006), experienced a natural disaster (Kilpatrick et al., 2007), or begun a stressful training program such as medical internship (Sen et al., 2010) or military basic training (Joiner & Schmidt, 1998). Another approach assesses individuals only after an event without a pre-event baseline for comparison (e.g., job losses; Howe et al., 2016), but this presents interpretive problems. It is challenging to examine stressful events as they unfold in part because it is difficult to predict when such rare events—especially major, negative events—will occur. One approach may be to enroll a very large sample that completes baseline measures and frequently (e.g., weekly) responds to event screenings, but only completes more intensive measures once study staff conclude a major event has occurred. Such an approach may be readily possible using automated screening tools available to researchers.

Third, the relationship of event severity, type, and number to the clinical *characteristics* of depressive episodes has been insufficiently examined. One effort using the LEDS in 100 individuals diagnosed with current depression showed that experiencing a severe event prior to depression onset (versus no severe event) was associated with greater episode severity, heightened cognitive and somatic symptoms, and greater life impairment (Muscatell, Slavich, Monroe, & Gotlib, 2009). Additionally, a large-scale effort examined participants who had experienced depression symptom episodes across four interview assessments (Keller, Neale, & Kendler, 2007). This study assessed symptoms of depression and self-indicated “causes” of the symptoms (including whether the symptoms began “out of the blue”) which were then coded by interviewers, a drawback that might have introduced bias. A between-person analysis of 3,137 individuals experiencing only one symptom episode and an independent within-person analysis of 1,719 individuals with multiple symptom episodes came to remarkably similar conclusions. Relationship

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losses predicted sadness, anhedonia, and appetite loss, while failure events and chronic stressors predicted hypersomnia and fatigue, and episodes emerging “out of the blue” predicted increased appetite, fatigue, and self-harm ideation. These efforts suggest this is a promising future direction that has been insufficiently explored. In particular, it may be useful to examine the influence of various types of stress on empirically supported symptom clusters or dimensions, consistent with recent efforts to inform dimensional outcomes such as impaired positive valence functioning that are relevant to depression but also cut across diagnoses (e.g., Cuthbert & Insel, 2013). Such an approach to stress and depression research may be likely to illuminate mechanistic pathways. Next, we turn to chronic stress.

Evidence for the Influence of Recent Chronic Stress in Adulthood

We first examine the historical underpinnings of objective chronic stress assessment, then methodological challenges, followed by a review of evidence, and last, future directions for this area. We hold that assessing chronic stress presents perhaps even more methodological challenges than assessing events, and that historical methodological heterogeneity and limitations have led—with unclear scientific merit—to diminished enthusiasm for studying chronic stress.

Historical Overview

Early chronic stress measurement was marked by pronounced heterogeneity and methodological limitations, which have likely led to widely varying estimates of chronic stress potency for depression. As noted earlier, Brown and Harris (1978) linked chronic difficulties to depression onset, but based on their impressions of the data, they concluded that the link between major difficulties and depression did not appear to be as robust in their original study (1978) nor as consistent across a series of later LEDS investigations (1989) as the link between severe events and depression. Consistent with their interpretation, at least one LEDS investigation failed to link major chronic difficulties with depression onset in the absence of a severe event (G. Brown et al., 1995). In contrast to the LEDS approach to conceptualizing major difficulties (i.e., present or absence of a problem lasting 2 or more years, rated in the more severe half of a 6-point scale, and not involving health problems), another approach, Hammen’s UCLA Life Stress Interview (LSI; Hammen et al., 1987), conceptualized chronic stress dimensionally as a range from the best possible quality of life to the poorest quality of life assessed in 8 to 10 domains (e.g., close friend relationship, family relationships, finances). In the LSI, the interviewer assigns a single chronic stress score for each domain for the entire period assessed, often the most recent 6 or 12 months. The LSI has been used to show that chronic stress predicts symptom worsening among already depressed individuals (Hammen, Davila, Brown, Ellicott, & Gitlin, 1992), and that chronic stress also predicts depression in a younger at-risk sample (Hammen, Shih, & Brennan, 2004). Still other research has operationalized chronic stress as the presence or absence of a single risk factor without accounting for contextual factors that make stressor severity differ

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between individuals. This approach may have contributed to disparate results; for example, while poverty (yes/no) predicted first onsets of depression (Bruce & Hoff, 1994), having a disabled child (yes/no) was not associated with lifetime or current rates of depression (N. Breslau & Davis, 1986).

Methodological Challenges in Chronic Stress Research

Beyond measure heterogeneity, there are several specific methodological challenges facing chronic stress assessment that may have hampered progress in establishing it as an important contributor to depression. First, failing to assess chronic stress over a wide array of areas (in contrast to the LEDS and LSI) is likely to underestimate its impact (Mazure, 1998). Second, we suggest that the dichotomization of even major chronic stress as present or absent, as opposed to using a dimensional severity scale, reduces power (Cohen, 1983; MacCallum, Zhang, Preacher, & Rucker, 2002), which may have contributed to the inconsistent effects Brown and Harris (1989) and others (N. Breslau & Davis, 1986) have observed. We acknowledge, however, that dichotomization does not appear to lead to inconsistent results for recent major events, suggesting the problem for chronic stress might be due to a combination of dichotomization and weaker true effect sizes. Third, when dimensional indicators such as those in the UCLA LSI are used ranging from best to worst possible quality of life, despite their likely advantage for power, results do not indicate whether good conditions are protective or bad conditions are hazardous (or both in a truly dimensional manner) without follow-up analyses.

Fourth, the LEDS classifies major difficulties as independent, possibly independent, or dependent—akin to the LEDS classification for events—although all forms of major difficulties significantly discriminated those with depression onsets and those without onsets, with similar relative risk scores in one analysis (Surtees et al., 1986). We suggest, however, that because of the challenge of ruling out that a person's behavior (potentially years ago) did not contribute to their chronic stress level, all forms of chronic stress should be conceptualized as *potentially* dependent—inextricably intertwined with the individual's characteristics, abilities, behaviors, and level of functioning. For example, chronic severe marital difficulties depend on the interpersonal interactions of two individuals. Indeed, some have observed that overlap of chronic stress and functioning level is particularly evident in the LSI partly because it captures the full range of quality of life (Harkness & Monroe, 2016), but we speculate that this is true of all chronic stress measures.

Fifth, it is important to note that the temporal precedence of chronic stress to depression onset cannot be ascertained in some studies that simultaneously assess recent chronic stress and depression. For example, the LSI yields a single score per life domain for the time period covered in the interview (e.g., past year) and would overlap temporally with depression diagnosed within that same interview window, regardless of how carefully the depressive episode is dated. Thus, in multiwave studies, an LSI from a prior wave can be used to establish temporal precedence (e.g., Hazel, Hammen, Brennan, & Najman, 2008). By contrast, because the LEDS treats chronic stressors as dichotomous constructs with

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discrete beginnings and endings, establishing temporal precedence is more readily accomplished.

Potency of Chronic Stress for Depression

Given the inconsistent early evidence and heterogeneous methods, perhaps it is not surprising that chronic stress has received less attention than major stressful life events in depression etiology research. This relative lack of research appears to have persisted despite reviews over an extended period of time arguing that the lack of focus on chronic stress is mistaken (Kessler, 1997) and calling for greater attention (Hammen, 2005). This lack of attention to chronic stress might suggest to readers that chronic stress's contributions to depression are significantly weaker than those of stressful events, but this is in fact unclear. This question remains inadequately tested.

Indeed, some evidence suggests that chronic stress may be as important as events; such results emerged from one large epidemiological study with more than 1,700 participants defining chronic stress as stressors beginning 12 months or more prior to the interview (McGonagle & Kessler, 1990). However, one limitation of this study's findings is the method of event ratings, which was not based on contextual threat. Rather, events were included if the event type was "typically" rated as high moderate to severe in its impact based on other research, similar to the approach used by Holmes and Rahe in their SRRS. It is likely this procedure led to the inclusion of a number of minor events, which have little impact, as well as the exclusion of some major events, thereby underestimating the true influence of events. Therefore, this particular approach may have *overestimated* the relative contribution of chronic stress. Furthermore, the use of self-reported depressive symptoms as the outcome also precludes establishing temporal precedence and hampers causal interpretation.

However, evidence for the importance of chronic stress has also emerged from limited studies using the LEDS and the LSI, both of which rate events contextually. Major difficulties (in this case, those in the upper *four* points of the LEDS 6-point scale) appeared to be as important for depressive episode onset as did acute events in a clinical sample of 50 Spanish individuals with depression and 50 controls (Rojo-Moreno, Livianos-Aldana, Cervera-Martinez, Dominguez-Carabantes, & Reig-Cebrian, 2002). It should be noted, however, that this outcome may in part be due to the authors excluding dependent events from analyses in an effort to heighten causal certainty. Similarly, dimensionally rated interpersonal LSI chronic stress was a significant unique predictor of depressive episode onset over and above several other forms of stress (including major interpersonal events, which were also a significant unique predictor) in two samples of emerging adults studied using the LSI (Vrshek-Schallhorn et al., 2015). Critically, however, neither of the former two studies aimed to test the difference in effect sizes between chronic stress and major events for predicting major depression. Thus, it is not possible to make statistical inferences about their relative contributions, but it is clear from Vrshek-Schallhorn et al. (2015) that interpersonal chronic stress contributed significantly to depression prediction even after accounting for major interpersonal events. Future efforts examining how multiple forms of stress predict depression should expand on this evidence. Thus, while it is apparent from both smaller samples using gold-standard stress assessment methods

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and from large epidemiological samples that chronic stress is an important contributor to depression, its precise relative contribution as compared to events remains an unresolved empirical question.

Chronic stress may also be important for its action through pathways other than a direct, independent path to depression; it may moderate other vulnerabilities and it appears to predict depression course. One study showed an interaction that approached significance in which chronic stress amplified the impact of interview-assessed events (Hammen et al., 2009). Chronic stress also appears to be associated with a more recurrent course of depression. In a diverse sample of 96 adults with current depression, the presence of major difficulties was associated with a greater number of prior depressive episodes (Monroe, Slavich, Torres, & Gotlib, 2007). Similarly, chronic stress has been shown to predict increased symptom growth over time in already depressed individuals (Hammen et al., 1992).

Interim Summary and Future Directions for Chronic Stress

We continue to advocate for greater attention to chronic stress, particularly through studies specifically designed to test the influence of chronic stress across a range of life domains on depression, ideally using repeated measures or other approaches to establish temporal precedence. Such “purpose-built” studies will avoid interpretive challenges of some large-scale epidemiological research using less intensive measures. Even *if* the impact of chronic stress is somewhat less robust than that of major events, as might be implied by the relative lack of research conducted on it, existing work does suggest that chronic stress represents an important factor in depression’s etiology for many individuals. Given how common and costly depression is, chronic stress is an important public health variable worthy of increased attention. Moreover, it is not necessarily true that chronic stress contributes less robustly than events to depression’s etiology. Testing the difference in the variance each contributes—particularly in large, generalizable samples using dimensional measures—is an important future direction for life stress research. Next, we turn to evidence for the stress-depression relationship in younger populations, covering more evidence on events, consistent with the literature.

Recent Stress Impacts Depression in Adolescents

The occurrence of depression among youth increases significantly during adolescence, particularly at age 14 onward (assessed as the 12 months prior to age 15; Hankin et al., 1998), rendering this period critical for etiological investigation. In an early study extending stress and depression work in adults to adolescents, Goodyer and colleagues (1985) found that adolescents in all diagnostic categories—including those diagnosed

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with depression—had experienced more interview-assessed recent, severe events prior to disorder onset compared to a matched period of time in controls. Over the past three decades, subsequent empirical investigations have further characterized the stress–depression relationship in adolescents, focusing more on events than chronic stress like the adult literature, with the goals of identifying the potentially causal and maintaining roles of stress in depression, as well as characterizing the specific forms of stress that exert an especially potent influence. Much of the work in this area also characterizes the contributions of various forms of interpersonal stress, although as is true for the adult literature, few papers test the difference in effects between multiple forms of stress.

Several interview-based studies provided additional support for stress in depression without attempting to establish particularly potent forms of stress. One such study, a 5-year longitudinal investigation employing the LSI that followed women during the transition from late adolescence into emerging adulthood, established both recent episodic and chronic stress as significant predictors of prospective depression (Daley, Hammen, & Rao, 2000). In this study, heightened levels of episodic stress measured across various life domains over the preceding 3 months increased risk for depression onset. Additionally, elevated chronic stress in the same 3-month period increased the likelihood of first onsets but not recurrences of depression. Similarly, work using an interview-based stress measure further supported that adolescents with depression experienced heightened levels of recent, acute stress prior to onset compared to controls (Williamson et al., 1998).

Attention to Interpersonal Stressors in Adolescents

Interpersonal theories of depression and empirical findings highlight that interpersonal stress is a potent predictor of depression among youth (for a review, see Rudolph et al., 2000). While few studies directly test the relative strengths of interpersonal and noninterpersonal stressors as predictors or correlates of depression, one such cross-sectional interview-based study did so. It revealed that among an outpatient clinical sample of youth (ages 8–18), dependent, interpersonal episodic events and chronic stressors were significantly more strongly associated with current depression symptom severity than their respective noninterpersonal counterparts in tests of dependent correlations (Rudolph et al., 2000).

Several studies establishing temporal precedence provide evidence for the potency of interpersonal stress in depression, although again without testing the difference between interpersonal and noninterpersonal stress. First, interview-assessed major disappointments (including such events as romantic breakups and academic failures) and interpersonal losses (deaths and permanent separations) in the prior month (but not events capturing danger to oneself or close others) predicted major depressive episode onsets in 12 to 16 year olds (Goodyer, Tamplin, Herbert, & Altham, 2000). Second, in a sample of emerging adults (ages 18–21) with a history of depression, those experiencing

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greater interview-assessed recent chronic interpersonal stress were at heightened risk for prospective depression recurrence, while noninterpersonal chronic stress did not predict recurrence (Sheets & Craighead, 2014).

Third, in a study following youth over 3 years, maladaptive response styles (i.e., greater endorsement of nonvolitional reactions, such as rumination, and lesser use of higher order, approach-oriented coping strategies, such as problem solving, assessed by questionnaire) to interview-assessed interpersonal stressors at baseline predicted greater stress generation—specifically heightened dependent, interpersonal events—over the subsequent 2 years. In turn, this generated dependent, interpersonal stress was associated with greater past-month depression symptom severity at a 3-year follow-up (Flynn & Rudolph, 2011). Notably, interpersonal stress, but not noninterpersonal stress, mediated the relationship between maladaptive baseline stress responses and later depressive symptoms. Fourth, elevated chronic family stress—one form of interpersonal stress—at baseline among older adolescent women predicted greater likelihood of experiencing a first onset of depression over the subsequent 2-year period (Eberhart & Hammen, 2006). Fifth, in a 6-year interview-based study of adolescents (the overall goal of which was to evaluate certain diathesis-stress interactions), both interview-assessed interpersonal and noninterpersonal achievement-related events separately predicted the first onset of a major depressive episode (Carter & Garber, 2011); however, this study neither simultaneously tested the stressors nor compared their effect sizes. From these five studies, it is clear that interpersonal stressors significantly and prospectively predict depression onset, although it is not possible to conclude from the available literature that the forms of interpersonal stress tested are significantly more potent than their noninterpersonal counterparts.

Within the domain of interpersonal stressors, romantic attachment-related stress has emerged as particularly salient for adolescent populations. In exploratory analyses of two samples beginning in late adolescence, the romantic stress domain of interview-assessed chronic stress was the only statistically unique predictor of the onset of major depressive episodes when simultaneously tested with other interpersonal domains of chronic stress in both samples (Vrshek-Schallhorn et al., 2015). Though exploratory, this finding complements previous work examining relationship status and depressive symptoms in adolescents. Among those in romantic relationships, those with a more preoccupied relational style—a form of insecure attachment marked by low trust, high dependence, and difficulty regulating emotions—experienced increased severity of depression symptoms (Davila, Steinberg, Kachadourian, Cobb, & Fincham, 2004). Furthermore, questionnaire-assessed romantic breakup events appeared to play a role in initial depression onset—but not significantly in recurrences—among high schoolers (Monroe, Rohde, Seeley, & Lewinsohn, 1999). Critically, these breakups contributed significant unique variance to risk for a major depressive episode over and above other questionnaire-assessed life events and daily hassles.

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Taken together, there is good evidence from studies able to ascertain temporal precedence that stress precipitates depression in adolescents. Although research has focused on interpersonal stress, sometimes specifically romantic stress, future research should work to show that these forms of stress are significantly more potent than other forms of stress.

Recent Stress Impacts Depression in Childhood

The study of depression in childhood represents a relatively young field compared to parallel efforts in adolescent and adult populations. Extant research suggests that exposure to stress predicts various maladaptive outcomes, including depression, in children. Moreover, diverse forms of recent stress, including events and chronic stress in a variety of life domains, have been associated with childhood depressive symptoms and diagnoses. Notably, studies of the effects of stress on childhood depression often examine depression symptom severity rather than depression diagnoses, given greater assessment challenges and lower rates of diagnoses in children as compared to adolescents or adults.

Focus on Events

Evidence for the role of recent episodic stress in depression among children comes from a number of studies representing samples at different stages of child development, but across all of these studies, longer timeframes following events are used than the comparable adult and adolescent literatures. In an investigation of risk factors for psychiatric disorders among daughters (ages 9 to 14 at baseline) of depressed and healthy mothers, daughters of depressed mothers were more likely to develop a disorder—in most cases, major depression—over the subsequent 30 months. Importantly, the children of depressed mothers who developed psychopathology including depression in this study reported heightened interview-assessed *dependent* events, but not *independent* events over the study period (Gershon et al., 2011). Several studies also suggest associations between stressful life events and depression in samples as young as preschool age. In the first prospective longitudinal study investigating the onset of depression in this age group, both early and recent episodic stressors reported through interviews by primary caregivers significantly predicted depression diagnosis at age 6 (Bufferd et al., 2014). Further, heightened questionnaire-based mother reports of child exposure to events in the year prior to baseline predicted greater severity of preschoolers' depression symptoms 6 months after baseline (Luby, Belden, & Spitznagel, 2006), and heightened past-year exposure to interview-assessed stressful events predicted prospective increases in an internalizing scale which includes depression symptoms (Kushner, Barrios, Smith, & Dougherty, 2016).

Interpersonal Stressors

Additional research on the stress–depression relationship in childhood focuses on individual interpersonal domains, such as family and peer functioning, which are known to influence development. As in the adult and adolescent literatures, however, studies have not tested the difference in potency between targeted forms of stress and other forms. For example, in the context of a gene–environment interaction study, baseline levels of interview-assessed chronic family stress did not act independently but interacted with a certain potential genetic risk factor for depression under stress, the serotonin transporter polymorphism, to predict depressive symptoms at a 6-month follow-up (Jenness, Hankin, Abela, Young, & Smolen, 2011). Of note, although this sample included a combined sample of children and adolescents (ages 7–16), the effect of chronic family stress in conjunction with genotype held for both developmental periods. Providing additional evidence for the role of family functioning in childhood psychopathology, a longitudinal investigation following caregivers and their children from 7 months to 3 years of age found that questionnaire-assessed self-reported harsh parenting and maternal stress at baseline significantly predicted both internalizing and externalizing symptoms in offspring (Bayer, Hiscock, Ukoumunne, Price, & Wake, 2008).

Interpersonal stress in the peer domain has been a focus of research for children and adolescents. A longitudinal investigation with youth ages 7 to 16 demonstrated that, among younger participants, greater interview-assessed chronic stress in peer relationships over the 3-year study period heightened risk for the onset of major depression or a significant subclinical manifestation (Hankin et al., 2015). Additionally, extensive research not reviewed in detail here has considered the role of a particular form of peer stress—peer victimization—in depression, with evidence to support a significant association between such experiences and depressive symptoms among children (for a review and meta-analysis of cross-sectional studies predominantly using questionnaires, see Hawker & Boulton, 2000).

Collectively, this work suggests a predictive role for various forms of stress in both childhood and adolescent depression. In particular, interpersonal stressors—including those experienced in relationships with family members and peers—have been a focus of research, although direct tests of greater potency are lacking. Moreover, when considered with findings in older samples, interpersonal stress confers risk for depression across the life span.

Interim Summary of Recent Stressors Across the Life Span

Taken together, there is strong evidence that recent, stressful life events prospectively predict depression symptoms and diagnoses across the life span. The contextual threat assessment approach of Brown and Harris (1978) rescued life events and depression research from the pessimistic conclusions generated by Holmes and Rahe's questionnaire methodology, and thus should be a continued focus of current work. There is a smaller body of evidence implicating interview-assessed chronic stress in depression symptoms and diagnoses across the life span, and this literature has been hampered by methodological heterogeneity and other limitations which should be addressed in future research. As we have alluded to throughout the section on recent stress, a theme cutting across stressors that researchers have suggested might be particularly potent (humiliation, loss, bereavement, targeted rejection) is their interpersonal nature. Direct tests of differential potency are limited, but those available support that interpersonal stress is significantly more potent than noninterpersonal stress. Thus, as discussed in detail later, a critical future direction for stress research will be to test the difference between the effects of stressors thought to be more potent against theoretically less potent stressors. Next, we review evidence for how demographic factors influence stress exposure and stress vulnerability to depression.

Who Is Most Impacted by Recent Stress? Demographic Variables in the Stress- Depression Relationship

Most models of how stress contributes to depression acknowledge that people differ in their vulnerability to stress due to pre-existing factors (diatheses), and researchers have devoted considerable attention to these diathesis-stress or vulnerability-stress models. Other chapters in this text consider cognitive, personality, and genetic vulnerabilities. Here we consider whether demographic factors—gender, race and ethnicity, and socioeconomic status—influence the stress-depression relationship. In each of these areas, research has examined differences in stress exposure and stress vulnerability.

Gender and Stress in Depression

Research has reliably indicated that females are at approximately double the risk of developing depression compared to males (Nolen-Hoeksema, 2001). This gender difference emerges during the transition to mid-puberty (Angold, Costello, & Worthman, 1998) and is maintained throughout much of the adult life course (for a review, see Kuehner, 2003). Given the role of stressful experiences in precipitating depression, several theories propose that gender influences the stress–depression relationship through gender differences in exposure and vulnerability to stress.

Stress Exposure and Gender

The transition to adolescence is marked by physiological, hormonal, and social role changes (Cyranowski, Frank, Young, & Shear, 2000), and interview-based assessments document an accompanying increase in stressful experiences for both sexes (Rudolph & Hammen, 1999). The stress exposure theory posits that females experience more frequent stressors during this transitional period. Support for this theory comes from findings that while both genders report increases in stress during the transition to adolescence, females experience greater increases in stressful life events compared to males, whether stress is assessed with questionnaire (Ge, Lorenz, Conger, Elder, & Simons, 1994) or with interviews (Rudolph & Hammen, 1999), the latter of which also demonstrated that substantial increases in interpersonal, dependent stressors among girls accounted for the emerging gender difference in stress exposure. This domain-specific finding of increased interpersonal, dependent stressors in females has been replicated in a separate sample of adolescent females and shown to partially mediate the gender–depression relationship (Shih, Eberhart, Hammen, & Brennan, 2006). In a further study, significantly more females than males reported interview-assessed stressors focused on people in their social networks, a form of interpersonal stress, prior to depression onset in three age groups spanning adolescence to middle age, but not among those 50 years or older (Harkness et al., 2010). Taken together, evidence supports the importance of interpersonal stressors for females across adolescence and much of the adult life span.

Stress Vulnerability and Gender

In addition to evidence for differences in stress exposure, stress vulnerability theories posit that females have more depressogenic *responses* to stressors—possibly chiefly interpersonal stressors—and that this at least partly accounts for the gender gap in rates of depression. This view is empirically supported by studies showing that females experienced more distress (Rudolph, 2002) and depressive symptoms in response to interview-assessed interpersonal events (Shih et al., 2006), and more depressive symptoms in response to interview-assessed interpersonal conflict stress (Rudolph & Hammen, 1999) than did males. Moreover, higher levels of interview-assessed familial early adversity predicted greater depression symptoms after *mild* recent interpersonal

stressors in pubertal females and prepubertal boys, but not in pubertal males (Rudolph & Flynn, 2007).

Influence of Race and Ethnicity in the Stress and Depression Relationship

The prevalence of major depression also varies across racial and ethnic groups, prompting investigations into the roles of race and ethnicity—mainly in Black and White groups—in the stress–depression relationship. A full review of epidemiological studies is beyond the scope of this chapter, but we highlight a conundrum for depression researchers. Evidence reviewed next suggests greater stress exposure among Black compared to White groups, but lower prevalence of depression is found among African American, Caribbean Black, and non-Hispanic Black groups compared to non-Hispanic White groups (J. Breslau et al., 2005; Riolo, Nguyen, Greden, & King, 2005; Williams et al., 2007), although some studies report the opposite as well (Rodriguez et al., 2018).

Two main hypotheses provide a framework for investigating a possible moderating role of race and ethnicity in the relationship between stress and depression (George & Lynch, 2003). The first contends that stress exposure varies by social status, which is influenced in part by race and ethnicity (for evidence from questionnaire-based stress measures, see R. J. Turner & Avison, 2003; R. J. Turner, Wheaton, & Lloyd, 1995), while the second proposes that—assuming stress exposure is held constant—social groups differ in risk for maladaptive responses to stress due to their levels of certain vulnerability factors (Kessler, 1979).

Both hypotheses have garnered some empirical support, although we caution that this evidence base is exclusively cross-sectional and assesses stress with questionnaires. Supporting a stress exposure model, in a sample of African Americans and non-Hispanic Whites, race was no longer a significant correlate of current depressive symptoms (which, in this sample, were higher in the African American subsample than the non-Hispanic White subsample prior to covarying other factors) when questionnaire measures of traumatic events, recent episodic stressors, and chronic stressors were incorporated into the regression model. Each of these stressors was a significant correlate of depression, suggesting that depression symptoms are associated with heightened exposure to stress among both groups (Taylor & Turner, 2002). Additionally, regarding differential stress exposure, a potentially potent form of stress in the context of race and ethnicity is discrimination at both individual and institutional levels (Grote, Bledsoe, Wellman, & Brown, 2007). Evidence points to a noxious role for discrimination in depression: Heightened exposure increases both depressive symptoms (Hunter, Case, Joseph, Mekawi, & Bokhari, 2017) and the risk of experiencing a lifetime major depressive episode (Budhwani, Hearld, & Chavez-Yenter, 2015).

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Finally, research also provides partial support for a role for differential stress vulnerability when exposure level is held constant. Among a national sample of groups identifying as Black (including African American and Caribbean Black) or non-Hispanic White, exposure to stressful life events and race interacted when gender-specific models were considered (Assari & Lankarani, 2016). Black men exposed to stress were at significantly *lower* odds of a major depressive episode compared to White men exposed to stress; no such evidence was found among women, however. Lower maladaptive stress reactivity may in part account for the apparent paradox of higher levels of stress yet lower rates of depression in Black individuals, but a lack of evidence in women suggests other factors play a role.

Potential additional reasons for the contrast between higher stress exposure but lower depression rates among Black individuals may include group differences in socialization and beliefs about low mood, including mental health stigmas. Indeed, one meta-analysis indicated that mental health-related stigma was negatively associated with treatment seeking, and this was disproportionately true for ethnic minorities, including Black individuals (Clement et al., 2015). A recent commentary concluded that despite substantial efforts, empirically supported explanations for lower depression rates among Black individuals remain elusive (Breland-Noble & Griffith, 2017). Thus, this remains an area for future examination.

Although less research has examined other racial groups, the limited available evidence suggests that major depression also appears to be less prevalent among Asian Americans compared to Whites (Budhwani et al., 2015). Prevalence differences, however, are not clear between Latino and White groups. Though a meta-analysis found no significant difference between the two groups (Mendelson, Rehkopf, & Kubzansky, 2008), the summary odds ratio (0.89) suggested a slightly but not significantly lower prevalence of major depression among Latinos. Furthermore, findings from a large-scale study published after the meta-analysis demonstrated significantly lower depression prevalence among Latinos compared to non-Latino Whites (Alegría et al., 2008).

Although more empirical work has focused on gender than race and ethnicity in stress and depression, similar themes of stress exposure and vulnerability have emerged (Assari & Lankarani, 2016; George & Lynch, 2003). Research from the race, ethnicity, and health disparities literature lends support to two apparent “paradoxes” related to stress exposure and physical health outcomes (but not yet mental health outcomes). For example, among older Mexican Americans, those living in neighborhoods with a higher percentage of Mexican Americans experienced lower prevalence of several medical conditions, including stroke and cancer, as well as lower mortality rates, despite exposure to greater poverty (Eschbach, Ostir, Patel, Markides, & Goodwin, 2004). This effect, known as the *barrio advantage*, suggests that protective factors related to social support mitigate the negative effects of poverty-related stress on health outcomes. These findings align with a larger body of research on the *Hispanic paradox*, which suggests similar or lower mortality rates among Latino groups compared to White groups despite greater

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exposure to environmental stressors related to lower socioeconomic status (for a review, see Franzini, Ribble, & Keddle, 2001).

Future research should investigate the relationship between differential exposure and vulnerability among more diverse samples and take racial and cultural socialization into account. Although evidence suggests a lower prevalence of major depression among racial and ethnic minority groups when compared to White groups, these findings should also be interpreted with the knowledge that prevalence of major depression varies by ethnic subgroup, nativity status, and age (Alegría et al., 2008; Budhwani et al., 2015; González, Tarraf, Whitfield, & Vega, 2010; Szaflarski et al., 2016).

Socioeconomic Status in the Stress-Depression Relationship

Evidence linking socioeconomic status (SES) and depression risk has been inconsistent. One meta-analysis identified no significant association between SES and depression symptoms in over 60,000 children completing the Children's Depression Inventory (Twenge & Nolen-Hoeksema, 2002), but a meta-analysis examining adults (> age 16) indicated that there is a modest yet significant effect of lower SES on increased risk for depression (Lorant et al., 2003). Further, a more recent estimate relying on over 43,000 in-person interviews significantly linked low SES with depression risk (Hasin, Goodwin, Stinson, & Grant, 2005).

Findings, however, are relatively consistent in linking lower SES with more frequent stressful events and higher chronic stress. One study using five self-report survey samples of approximately 700 to 2,000 people each found relatively consistent evidence that low SES weakly but significantly correlated with greater likelihood of self-reported negative life events across all aspects of life (McLeod & Kessler, 1990). Other findings indicate that low SES is associated with fewer interview-assessed coping resources, including having fewer close confidants (G. Brown & Harris, 1978). Further, evidence indicates that which *types* of stressors are most potent may vary across the SES spectrum. In an emerging adult sample, a significant interaction of interview-assessed noninterpersonal major events and SES indicated that this form of stress was relatively more potent for individuals of lower SES than those of higher SES. Further, interpersonal chronic stress was more impactful among higher SES individuals, while noninterpersonal chronic stress was more potent among lower SES individuals (Vrshek-Schallhorn et al., 2015). Major interpersonal events, however, remained potent precipitants of depression regardless of SES. Taken together, lower SES appears to modestly but significantly enhance risk for depression, and it appears to do so through modestly increased stress exposure and nuanced differences in vulnerability.

In summary, there is relatively consistent evidence for greater stress exposure among women, racial and ethnic minority groups, and lower SES populations, and this appears to account at least in part for the gender difference in depression. However, a puzzle

remains for future research to reconcile evidence of lower rates of depression among some minority groups with evidence of greater stress exposure and even stress sensitivity. Next, we turn our attention to the early adversity and depression literature.

Early Adversity Has Both Proximal and Distal Effects

“Early adversity” has been used to capture a heterogeneous group of negative and uncontrollable experiences of children and adolescents (<18 years old), ranging from more traditional examples such as exposure to maltreatment (including physical, sexual, and emotional abuse and neglect), death of a parent, and separation from a parent (see Table 1 for additional examples) to more broadly defined indicators such as parental psychopathology. Here we focus on more traditional forms of adversity and not parental psychopathology. This review first examines methodological factors that should be considered in evaluating the literature, then describes evidence for both proximal and distal effects of early adversity, explores evidence that certain forms of adversity are more potent than others, and discusses several pathways that may reconcile how early experiences can confer long-term impact.

Methodological Challenges for Early Adversity Research

There are three primary salient methodological issues in early adversity and depression research. First, many studies rely on designs in which adversity and depression history are simultaneously self-reported, which does not allow establishment of temporal precedence to ensure that stress precedes and therefore potentially causes depression. This challenge is salient for child and adolescent samples, in which the stress–depression association is more proximal, but in adults, this is not a concern when it is established that the first onset of depression occurred *after* the adversity.

Second, many studies understandably use retrospective reports of early adversity, partly because of mandatory reporting to social services when mental health researchers learn of the ongoing abuse of a minor, and partly because of logistic and funding challenges of conducting extended longitudinal research. Retrospective reports may be subject to forgetting or biased recall, perhaps particularly in clinical samples. However, some have argued that retrospective reports *under-* rather than overestimate adversity’s occurrence, suggesting that retrospective reports actually provide a relatively conservative adversity measure (for a review, see Hardt & Rutter, 2004). Similarly, evidence suggests that psychopathology does not bias reporting (for a review, see Brewin, Andrews, & Gotlib, 1993).

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Third, the quality of assessment varies widely. As in the recent stress literature, interview-based contextual assessment of adversity offers substantial advantages over self-report checklist measures of adversity. Of the available interview tools (for a review, see Roy & Perry, 2004), the Childhood Experiences of Care and Abuse (CECA; Bifulco, Brown, & Harris, 1994) interview, a counterpart of the LEDS, has the advantage of yielding ratings of severity blind to the participant's response. One alternative to retrospective self-reports is to rely on substantiated or documented cases of abuse using official records (e.g., social service agency records). However, this approach also poses challenges to generalizability because these reports likely represent the most severe cases of adversity. Moderate severity adversity (severe enough to cause harm, but unlikely to be discovered and reported to authorities) may be overlooked. Such omissions would contribute to underestimating the impact of the full spectrum of adversity severity. Considering each of these concerns, it seems that there is no one approach that is completely without drawbacks. Scientists then do well to prioritize longitudinal research with interview measures and to pursue replication across methods.

Proximal Effects of Child Maltreatment

Maltreatment is associated with a range of near-term negative outcomes in youth (for reviews of this expansive area, see Springer, Sheridan, Kuo, & Carnes, 2003; Staudt, 2001), and several studies using documented abuse provide evidence for a significant relationship between recent maltreatment in children and depression. First, in a study comparing individuals in middle childhood with a history of prior maltreatment (abuse and neglect documented in official records) to those without such history, experiences of physical abuse and physical neglect predicted higher self-reported depressive symptoms at baseline (Kim & Cicchetti, 2006). Second, a large-scale study conducted in Australia examined the effects of childhood sexual abuse using all records of reported sexual childhood abuse cases and subsequent contacts of the 2,759 victims with the public mental health system over a 31-year period, as compared to those of age- and gender-matched (but otherwise randomly selected) controls drawn from the electoral database. Diagnostic records showed that individuals with a history of childhood sexual abuse were at significantly elevated risk for a range of psychiatric disorders, including depression, both in youth (prior to age 18) and in adulthood, compared to controls (Cutajar et al., 2010).

Childhood Adversity Also Has Distal Effects on Depression During Adolescence and Adulthood

Consistent evidence for the etiological role of early adversity in later depression comes from three decades of research in (1) large epidemiological studies using primarily questionnaire measures (Felitti et al., 1998; Kessler, Davis, & Kendler, 1997), (2) twin studies using questionnaire assessment of sexual abuse (Kendler et al., 2000), and (3) large birth cohort studies utilizing a combination of interviews and questionnaires (Jaffee et al., 2002), among other evidence. Aggregating this work, three separate meta-analyses concluded that exposure to significant early adversity (e.g., physical abuse, sexual abuse, or neglect) significantly increases the risk for depression in adulthood, with pooled odds ratios ranging from 1.49 to 3.06 across various forms of adversity in the three meta-analyses (Li, D'Arcy, & Meng, 2016; Lindert et al., 2014; Norman et al., 2012). Li et al. (2016) is particularly noteworthy for its exclusion of studies that relied on retrospective self-reports of maltreatment, and seven of eight studies included used reviews of official records.

Early adversity's association with increased risk for later depression also spans both adolescence and adulthood. The most robust causal evidence that adversity during childhood leads to later depression comes from prospective research. For example, in a large ($N = 639$) 17-year prospective study of official records-based cases of physical abuse and neglect and retrospectively self-reported sexual abuse, maltreated individuals exhibited an increased risk of developing depression during adolescence and early adulthood compared to nonmaltreated individuals (J. Brown, Cohen, Johnson, & Smailes, 1999). Further, in a prospective birth cohort study ($N = 998$), higher childhood adversity exposure (e.g., parental criminality, loss/separation, or psychopathology) assessed through a combination of questionnaires and interviews was associated with juvenile-onset depression (10–14 years), although not significantly with first onsets of depression in emerging adulthood (17–25 years of age), which could be consistent with declining impact as time passes after the adversity (Jaffee et al., 2002). Contrasting this latter finding, in other prospective research, early adversity has been linked to depression during adulthood. In one prospective cohort study, over 600 individuals with documented cases of early adversity (physical abuse, sexual abuse, or neglect) were at increased risk for current and lifetime depression diagnoses compared to over 500 demographically matched nonabused controls, although effects fluctuated somewhat by type of adversity (Widom, DuMont, & Czaja, 2007).

Early Adversity Influences Depression Course

Early adversity not only impacts depression occurrence but also influences the clinical course of the disorder, including the frequency of recurrences, age of onset, and duration of episodes. A meta-analysis examining frequency of episode occurrence showed that, in 16 epidemiological samples with more than 23,000 combined participants, childhood

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maltreatment was associated with recurrent or persistent depression with a 2.27 combined odds ratio (Nanni, Uher, & Danese, 2012). One study is particularly compelling for its use of the CECA interview among a sample of sister pairs, in which parental maltreatment was associated with greater rates of chronic depression. In the sister pairs that were discordant on maltreatment, the maltreated siblings experienced a greater increase in risk for chronic depression compared to their nonmaltreated siblings (G. Brown, Craig, Harris, Handley, & Harvey, 2007). Further, a history of childhood sexual abuse, physical abuse, and neglect has been shown to predict significantly earlier age of depression onset in studies with questionnaire measures (Bernet & Stein, 1999) and those based on official records (Widom et al., 2007). Additionally, interview-assessed early adversity was associated with longer episodes (Zlotnick, Mattia, & Zimmerman, 2001).

Childhood adversity has also been linked to poorer depression treatment outcomes. In a meta-analysis using 10 clinical trials comprising more than 3,000 combined participants, childhood maltreatment history was associated with poorer treatment response to both psychotherapy and medication compared to those without such history, with a 1.43 combined odds ratio (Nanni et al., 2012). In one study that examined the relative effectiveness of several treatments for those who have experienced prior maltreatment (ascertained by questionnaire), psychotherapy was significantly more effective at treating depression than medication alone, and adding medication to psychotherapy did not provide significant benefits beyond psychotherapy alone (Nemeroff et al., 2003). Taken together, this evidence supports that not only is childhood adversity associated with greater rates of depression, it also impacts important clinical outcomes of persistence, recurrence, and treatment response.

Content of Adversity During Early Development

There has been considerable discussion regarding which types of adversity might be most noxious in the etiology of depression. One hypothesis is that emotional abuse such as verbal aggression and emotional neglect may increase risk for depression more than other types of adversity by directly providing negative content to a child (e.g., “You are worthless”), contributing to the development of negative self-schemas (Rose & Abramson, 1992), as supported by one quantitative review using a combination of self-reports and official records (Gibb, 2002). Evidence for the potency of emotional abuse comes from studies examining different forms of early adversity, which have found that emotional abuse was significantly more strongly associated with depression compared to other types of maltreatment when assessed by questionnaire (Gibb, Chelminski, & Zimmerman, 2007) and when assessed by interview (Lumley & Harkness, 2007; Spinhoven et al., 2010). Similarly, neglect is hypothesized to activate loss-related schemas, as supported by a study using the CECA interview (Lumley & Harkness, 2007), and to sensitize individuals to later dependent stress, assessed with a questionnaire in one supportive study (Shapero et al., 2014). A meta-analysis of 12 CECA studies provides some support for these hypotheses, such that psychological abuse had the largest descriptive effect size (defined as coercive control; Cohen’s $d = .93$), followed by physical and emotional neglect ($d = .81$). Further, these effects did not overlap the 95% confidence intervals of several other forms of abuse, including sexual abuse ($d = .50$) and antipathy (coldness, hostility; $d = .51$), supporting greater potency for psychological abuse and neglect in depression (Infurna et al., 2016).

There is also evidence that the effects of different types of early adversity vary by gender. A large ($N = 34,653$) representative sample of the US population was assessed using retrospective questionnaires of early abuse and neglect and lifetime diagnostic interviews for internalizing (anxiety, depression) and externalizing disorders (addiction, antisocial personality). A latent variable analysis demonstrated that, among both genders, emotional abuse was significantly more strongly related to latent internalizing than to externalizing. Further, among women, physical abuse was significantly more strongly related to internalizing than to externalizing, while among men, physical abuse was more strongly related to externalizing than to internalizing—the latter a particularly sharp contrast with results for women (Keyes et al., 2012). Similarly, among men, sexual abuse was more strongly related to internalizing, whereas among women, it was related significantly to both internalizing and externalizing, but the strength of the two paths did not significantly differ.

Impact of Adversity Timing During Childhood and Adolescence

In addition to discussion of the most potent forms of early adversity, there has been discussion regarding whether earlier childhood adversity is more potent than later childhood or adolescent adversity for the etiology of depression, but this evidence base is

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somewhat inconsistent and usually does not test the difference in effects between developmental periods. The hypothesis that earlier adversity is more potent than later adversity reasons that earlier adversity interferes with the successful development of emotion regulation and attachment style (for reviews, see Baer & Martinez, 2006; Cicchetti & Toth, 1995), cognitive processes (for a review, see Beck, 2008), and biological systems (for a review, see Heim, Newport, Mletzko, Miller, & Nemeroff, 2008) required for later adaptive psychological functioning. Evidence consistent with that view comes from a study using baseline physical harm interviews and annual follow-up questionnaires predicting internalizing symptoms in eighth grade (Keiley, Howe, Dodge, Bates, & Pettit, 2001) as well as from a study examining official records (Manly, Kim, Rogosch, & Cicchetti, 2001). Additional support comes from a prospective study of abuse and neglect in official records, which demonstrated that adversity during earlier developmental periods (i.e., infancy through preschool age; 0–5 years) was more strongly associated with increased depressive symptoms in adulthood than was adversity experienced later in childhood (6–11 years; Kaplow & Widom, 2007). Last, in a large ($N = 907$) longitudinal study of maltreatment documented through official records, although adversity limited to childhood (0–11 years) showed overall fewer significant associations with a range of negative outcomes than adolescent adversity, adversity limited to childhood predicted questionnaire-based current depression symptoms in early adulthood, while adolescent adversity did not (Thornberry, Henry, Ireland, & Smith, 2010).

Not all evidence, however, supports that early adversity is more potent than later adversity. For example, in a study utilizing official records to document maltreatment and interviewing victims within 8 weeks of discovery, age at discovery of sexual abuse predicted depression symptoms, such that adolescents had greater depression symptoms, which may be due to the surge in depression symptoms observed in adolescents or to adolescents' more advanced cognitive development (Feiring, Taska, & Lewis, 1998). Indeed, in this study, feelings of shame and cognitive attributional style partly accounted for the observed association between age and depression. A further study utilizing retrospective interviews of early adversity found that, when including both childhood (age 0–9) and preadolescent to adolescent (age 9–16) interview-based adversity as predictors, only later adversity contributed significant unique variance in the prediction of first depression onsets during late adolescence and early adulthood, potentially due to the attenuation of the effects of earlier adversity over time (Vrshek-Schallhorn, Wolitzky-Taylor, et al., 2014).

What Might Account for the Paradoxical Long Action of Early Adversity?

Although there is broad evidence for the association between early adversity and depression in adulthood, many studies examining this relationship do not assess or simultaneously report on *recent* life stress, which would permit examination of whether early adversity contributed statistically unique effects above and beyond recent stress. Some scholars have proposed a stress-recency model (Shanahan, Copeland, Costello, & Angold, 2011), which posits that stressors pose a time-limited risk, such that they are most potent shortly after occurrence and decline in potency as time passes, consistent with the adult event literature. In line with this, interview-assessed childhood adversity predicted childhood-onset depression more strongly than it did adult-onset depression, while adult-onset depression was most strongly associated with adversity in adulthood (Shanahan et al., 2011).

This stress-recency model poses an intriguing question: If the effects of stressful events for depression are most noxious shortly after event occurrence and abate soon thereafter, how can this be reconciled with evidence that adversity persistently increases risk for depression occurrence years, even decades later? One possibility is that early stress may make individuals more vulnerable to later stress even in milder forms (stress sensitization theory; Monroe & Harkness, 2005). The implication is that even when early adversity does not quickly provoke depressive onsets, such experiences leave individuals more vulnerable to the effects of later—possibly less severe—stressors. In support, individuals with a history of interview-assessed maltreatment have been shown to be more likely to report *less severe life stress* prior to depression onset compared to those without such history (Harkness, Bruce, & Lumley, 2006). Additionally, pubertal girls and prepubertal boys (but not prepubertal girls and pubertal boys) who experienced questionnaire-assessed family disruption or loss exhibited more depressive symptoms in response to later interview-assessed interpersonal stressors compared to controls (Rudolph & Flynn, 2007), and individuals who experienced interview-assessed early parental loss demonstrated greater sensitivity to later interview-assessed interpersonal losses (Slavich, Monroe, & Gotlib, 2011), suggesting that early stress not only sensitizes to later stress but also may do so in a congruent stressor-specific fashion. Finally, Hammen and colleagues (2000) demonstrated a significant stress sensitization interaction between early adversity and recent events in a sample of young women, such that those with a history of questionnaire-assessed early adversity were significantly more prone to depression in early adulthood under *lower* levels of interview-assessed recent episodic stress than their counterparts without early adversity. Under higher levels of recent event stress, early adversity did not further discriminate risk.

A second possibility is that early adversity leads to higher levels of chronic and acute stress later, a stress continuation or stress generation model. Some scholars have speculated that early adversity contributes to higher levels of later and ongoing stressors;

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thus, childhood adversity could be in part conceptualized as a risk for stress continuation. Support for this view comes from four studies showing that early adversity's relationship with later depression is mediated by more proximal stress. In a large epidemiological survey, the relationship between interview-assessed childhood family violence and recurrent depression was mediated by recent, adult chronic interpersonal stress (Kessler & Magee, 1994). Similarly, a study of over 600 participants using questionnaire measures found that recent stress mediated the association between childhood adversity and adult depression symptoms (H. A. Turner & Butler, 2003). These findings were replicated and extended by a study that showed the effects of early adversity on depression diagnoses were mediated by a composite score of recent interview-assessed events and chronic stress (Hazel et al., 2008). Finally, a fourth study showed that only recent interpersonal—not noninterpersonal—interview-assessed chronic stress mediated the relationship (Vrshek-Schallhorn et al., 2015).

In summary, the evidence shows that early adversity prospectively predicts depression, and it is associated with earlier onset, more frequent episodes, and poorer treatment responses. Although there is good support that emotional abuse has significantly greater effects on depression than other forms of abuse, there is mixed evidence regarding whether early childhood adversity is more likely to lead to depression than adversity occurring later in childhood or in adolescence. Finally, there is evidence that the relatively long action of early adversity might be due to stress sensitization effects or stress continuation effects, in which early adversity breeds adversity during adulthood. Key future directions include expanding upon these latter two possibilities and investigating how to interrupt stress continuation.

Future Directions

In addition to future directions we have identified throughout the chapter, here we discuss four overarching future directions for stress and depression research.

Assessment Quality Remains as Relevant as Ever Before

As we reviewed, prior to Brown and Harris's and their contemporaries' contributions to stress assessment, early efforts to characterize the stress-depression relationship produced unconvincing effect sizes and used assessment approaches that confounded vulnerability, symptoms, and objective exposure, among other issues. The critical methodological advancements (best practices) that resolved confounds and isolated etiologically potent stress were using (ideally blinded) investigators' rather than participants' judgments of event thresholds and severity, accounting for severity, establishing temporal precedence, and using time-sensitive approaches that isolate 1-3 months prior to depression onset. Unfortunately, the assessment approaches that include these advancements tend to require a great deal of investigator resources (training, personnel, supervision, and participant time) even to produce several hundred interviews. In an age of "big data" with datasets of 10,000 or more participants, and high demands for investigator productivity, we argue that life stress and depression research—including diathesis-stress interaction mechanistic research—will not progress further without continued use of these best practices. Nowhere has this been clearer than in gene-environment interaction research, where more robust interaction effects emerged for interview and other objective measures of stress than for questionnaire measures of stress (Karg, Burmeister, Shedden, & Sen, 2011). One potential solution is for life stress researchers to join together to use consensus best practice interviews to generate larger datasets.

Isolating the Most Potent Forms of Stress Will Aid Intervention and Basic Research Efforts

Just as learning that only major and not minor events significantly predicted depression led to progress in Brown and Harris's era, isolating the most potent forms of stress will lead to progress today. This is useful for at least two reasons: (1) knowing what forms of stress to target in preventive interventions and (2) minimizing multiple testing, boosting consistency across studies, and focusing resources wisely in mechanistic research such as diathesis-stress research and biological research on stress. Genetic research, for example, is particularly concerned with minimizing multiple testing due to the large number of genetic variants measured in some studies, an issue compounded by testing multiple forms of stress in interactions with genetic variants. There is also evidence that certain biological systems are preferentially sensitive to certain forms of stress (Dickerson & Kemeny, 2004; Vrshek-Schallhorn, Mineka, et al., 2014), and identifying the most potent forms of stress for depression is likely to produce larger effect sizes when biological predictors of stress response or biological stress response outcomes are studied.

To identify the most potent forms, studies will first need to account for positive correlations between forms of stress, which can obscure which form is contributing statistically unique effects; this can be accomplished by including multiple forms of stress in the same statistical model. Studies will also need to test the difference in effect sizes between forms of stress predicting depression, for example through deviance tests, facilitated by modern statistical software platforms. In some cases, it may also be useful to characterize and validate new approaches to data reduction that account for total stress burden (e.g., Hazel et al., 2008), perhaps aggregating across relevant stressors (e.g., interpersonal chronic and episodic stress). These efforts should acknowledge that potent forms of stress may vary across development and demographic factors, given evidence that the potency of noninterpersonal stress varied as a function of SES (Vrshek-Schallhorn et al., 2015).

Life Stress and Depression Researchers Should Contribute to Depression Prevention and Intervention Efforts

Stress and depression researchers should increasingly turn their attention to translational efforts aimed at applying what has been learned from the past 40 years of research. First, they have the opportunity to offer a unique perspective. Too often, in popular culture and even in psychological science, stress is conceptualized as only the emotional *response* to circumstances, which suggests emotion regulation skill interventions for stress-related disorders. Stress and depression researchers can make the case that stress can also be conceptualized as objective experiences—the negative events and more chronic circumstances individuals face—which suggests the addition of problem-solving skills in interventions to modify the environment when objective stress is elevated. Second, stress researchers can also use evidence to point to the most noxious forms of stress as targets for intervention during treatment or in public health depression prevention efforts.

Third, stress researchers also can help pursue research on the effectiveness of interventions to interrupt stress continuation effects between childhood and early adulthood. Evidence that early adversity's influence on depression in adulthood is mediated by recent stress suggests that early adversity disrupts the formation of healthy life skills, including those vital to interpersonal functioning, which help keep later stress at bay. For example, the same adult caregiver who perpetrates emotional abuse on a child is likely to frequently model ineffectual and stress-generating interactions with other people. Thus, the same child who is victimized by emotional abuse may also be likely to approach adulthood with poorly developed interpersonal skills. Indeed, a study conducted exclusively among lower SES children in a Head Start preschool program indeed found evidence that maltreated children had poorer social skills than their nonmaltreated peers

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(Darwish, Esquivel, Houtz, & Alfonso, 2001). One potentially fruitful preventive intervention (or even treatment, post diagnosis) for individuals previously exposed to prior early adversity could be an adaptation of the interpersonal skills module used in Dialectical Behavior Therapy. At least one effort has augmented traditional exposure therapy with emotion regulation and interpersonal skills training to treat child abuse-related posttraumatic stress disorder with clear benefits (Cloitre, Koenen, Cohen, & Han, 2002), but similar efforts could be applied more broadly.

Greater Study of Race, Ethnicity, and Culture in Stress-Depression Research

Finally, although many of the samples in the studies we reviewed were diverse, objective stress and depression research has paid insufficient attention to race, ethnicity, and culture in the stress-depression pathway. Objective stress research should examine the contrast we observed (evidence of greater stress exposure but also lower rates of depression in Black compared to White individuals) as well as the influence of cultural factors in stress exposure and responding. Future research should also examine a wider array of minority groups, for example to understand acculturative stress in immigrant communities.

Conclusion

Taken together, evidence linking an array of forms and timings of life stress with depression is robust. The evidence for this relationship extends across the life span, with recent stress predicting depression symptoms and onsets at every age, and distal stress from childhood enhancing risk and worsening depression course years later in adulthood. Evidence for the relationship also extends across multiple forms of stress, but more research has focused on stressful life events than on chronic stress. We argue that this lack of attention to chronic stress is mistaken because there is evidence that chronic stress predicts depression even after stressful events are accounted for. The literature also provides early evidence consistent with a conclusion that several manifestations of interpersonal stress are more potent than other forms of stress, but studies have rarely carried out the decisive tests of effect size magnitude necessary to firmly draw this conclusion. Moving forward, stress and depression researchers should redouble their efforts to use best practice assessment techniques, work to isolate the most potent forms of stress, contribute to intervention and prevention efforts, and pay greater attentions to issues of race, ethnicity, and culture.

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