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Major Life Events and Major Chronic Difficulties Are Differentially Associated With History of Major Depressive Episodes

Scott M. Monroe, George M. Slavich, and Leandro D. Torres
University of Oregon

Ian H. Gotlib
Stanford University

Major life events have been found to precede onsets of a 1st lifetime episode of depression more commonly than subsequent recurrences. Despite general empirical support for this finding, few data directly address how the role of major life events may change over successive recurrences. Further, little research has examined major chronic difficulties in relation to a 1st lifetime episode versus a recurrence of depression. The present study tested the associations between major life events and major difficulties in relation to lifetime history of depressive episodes in a sample of 96 individuals diagnosed with major depression. Using investigator-based measures of life stress, the authors found that, whereas major life events were associated with fewer lifetime episodes, major chronic difficulties were related to more prior episodes. These findings are discussed in terms of underlying mechanisms that may account for the changing role of major life stress over successive recurrences of depression.

Keywords: life events, chronic stress, depression, recurrence

Major depression is one of the most common and one of the most disabling psychological conditions (Gotlib & Hammen, 2002). The impairment resulting from depression is severe, not only because of the pervasive impact of an episode of the disorder on the afflicted individual's life, but also because of the high likelihood that depression will recur, often repeatedly, over the life course. Considering cumulatively the high prevalence, the serious impairment, and the frequent recurrence of unipolar depression, this disorder represented the fourth leading cause of disability worldwide in 1990 and is expected to become the second leading cause of disability worldwide by the year 2020 (Murray & Lopez, 1996).

Over the past 2 decades, theoretical and clinical interest in the causes of depression has shifted from a predominant emphasis on acute, single episodes to a longitudinal perspective on the life course of depression. This shift is due largely to the emerging awareness of the high likelihood that people suffering from depression will experience repeated recurrences of the disorder over their lifetimes (Belsher & Costello, 1988; Hammen, 2005). Of particular interest is the distinction between a first lifetime episode of major depression and subsequent recurrences of the disorder. There are good reasons to consider the possibility that the factors that give rise to an initial episode differ in kind or in arrangement from those that play a role in subsequent recurrences. One especially promising area of focus for examining this issue is the relation between life stress and depression (Monroe & Harkness, 2005). A large and consistent body of research documents a central role for major life events in the onset of depression (Brown & Harris, 1989; Hammen, 2005; Mazure, 1998; Monroe & Hadjiyannakis, 2002). Within this general literature, it has become apparent that the etiological importance of major life stress changes following the onset of a first lifetime episode and over subsequent recurrences. Post (1992) was among the earliest researchers to note that major life stress appears to be associated more strongly with first episodes of major affective disorder than with later episodes. Subsequent reviews of the literature on life stress and major depression have generally supported this observation (Mazure, 1998; Monroe & Harkness, 2005; cf. Hammen, 2005). Investigating major life stress in relation to the initial onset and to the later recurrence of depression may provide insights into both the mechanisms that initiate and then perpetuate episodes of depression and the processes that accumulate and then eventuate in the extreme disability burden of the disorder.

Despite relatively consistent findings indicating a greater role for major life stress in the onset of initial lifetime episodes than in later recurrences, the theoretical rationale for this effect is not clear. Based on animal laboratory studies of electrophysiological kindling, as well as on research on stress and cocaine sensitization, Post (1992) proposed a framework of ideas to explain the development of episodic disorders that initially are stress related but that subsequently appear to emerge independent of stress. The basic premise of this "kindling hypothesis" is that repeated experiences of stress and depression render an individual more sensitized to the effects of stress and progressively more sus-

Scott M. Monroe, George M. Slavich, and Leandro D. Torres, Department of Psychology, University of Oregon; Ian H. Gotlib, Department of Psychology, Stanford University.

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Correspondence concerning this article should be addressed to Scott M. Monroe, who is now at the Department of Psychology, University of Notre Dame, 118 Haggar Hall, Notre Dame, IN 46556. E-mail: smonroe1@nd.edu

ceptible to the recurrence of depression. Consistent with this view, Post proposed a model that "presents a clear-cut example of the shift from episodes that are triggered to those that occur autonomously" (p. 1001).

It is important to note, however, that there is imprecision about the role of stress in this formulation, confusing a kindling and autonomy theme (i.e., stress becomes independent of the onset of depression) with a kindling and stress sensitization theme (i.e., lower levels of stress become capable of triggering recurrences; see Hlastala et al., 2000; Monroe & Hadjiyannakis, 2002). For example, whereas some investigators consider stress to diminish in importance with repeated episodes (as more autonomous neurobiological processes begin to dominate in the explanatory scheme), other investigators consider stress to increase in importance with repeated episodes (as sensitization lowers the threshold for stress needed to trigger episode onset). Indeed, in a recent theoretical review of life stress and the recurrence of depression, Monroe and Harkness (2005) detailed the widespread confusion and inconsistencies in the literature involving these two viewpoints.

Several lines of research may be pursued to help resolve these theoretical tensions. In the present study we address two timely issues. First, the literature on life stress and recurrence is based largely on studies that compare people with first lifetime episodes of depression with people with at least one recurrence. This means that people with one or more prior depressions are collapsed into the broad category of recurrence. This strategy potentially obscures the changing role of major stress over the extended clinical course of multiple recurrences. Consequently, it is important to determine whether differential associations of major stress with recurrence hold when formerly depressed individuals are stratified more precisely with regard to their lifetime histories of episodes. For example, are major life events differentially common prior to first, second, or third lifetime recurrences? At what point in the progression of recurrences does the importance of major life events before onset appear to change? More generally, it is useful at the present stage of understanding to develop more fine-grained descriptive data to portray how the association between major life events and recurrence evolves over repeated episodes (see Monroe & Harkness, 2005).

Second, the literature on life stress and recurrence is based predominantly on research involving acute life events. Few investigators have examined major chronic difficulties in relation to a first onset versus recurrence of depression (Hammen, 2005). Although major difficulties have been found to predict the onset of a depressive episode (Brown & Harris, 1978, 1989), there is limited empirical information to determine whether there is a differential association between major difficulties and first lifetime episodes versus between major difficulties and recurrences of depression. For example, Daley, Hammen, and Rao (2000) found an interaction between history of depression and chronic difficulties. Chronic difficulties predicted a first onset but not a recurrence of depression. Unfortunately, this is one of the few investigations, if not the only study, characterized by sound methods and research design that includes chronic stressors.

Examining chronic difficulties and recurrence also holds promise for illuminating basic theoretical issues involving life stress and depression. On the one hand, if there is an association between chronic difficulties and the distinction between first onsets and recurrences of depression, it might parallel the pattern found for major life events (i.e., chronic difficulties may be more common prior to the onset of earlier than of later episodes of depression). On the other hand, major chronic stress may operate in a complementary manner with major life events and be more prevalent with later recurrences. Indeed, this latter possibility is especially plausible given the stress-generation hypothesis (Hammen, 1991), which suggests that a history of depression leads to an increase in acute life events. Thus, it is theoretically consonant that stress-generation processes could be extended to and might eventuate in more chronic life stress as well.

Finally, given the importance of stress generation and its potential implications for recurrences of depression, it is also useful to evaluate the extent to which severe life events experienced by individuals are outside of or within their control (Hammen, 2005; Harkness, Monroe, Simons, & Thase, 1999). Independent severe events are events that occur independently of the individual's behavior, whereas possibly dependent severe events are events that are likely to occur at least in part owing to the person's actions. Accordingly, we also conducted secondary analyses to determine the extent to which associations between severe acute events and recurrence may be attributed to either independent severe events or possibly dependent severe events.

In sum, the present study was designed to address several issues that are critical for understanding the nature of the changing role of life stress over repeated episodes of major depression. First, we examine the role of severe life events and lifetime history of depression. Employing state-of-the-art diagnostic and assessment methods with a sample of 96 depressed persons, we predicted that a greater number of severe life events would be associated with a history of fewer depressive episodes. Second, we expand this prediction and add to the existing literature to provide a more differentiated statistical analysis and finer grained presentation of the changing prevalence of severe life events preceding onset, stratified by the number of lifetime episodes of depression. Third, we investigate the role of severe chronic difficulties to determine whether such forms of stress possess a similar or different pattern of association with lifetime history of depression. Finally, we conduct secondary analyses to ensure that the major findings cannot be attributed to other demographic or clinical correlates and to examine whether the major findings hold for major life events that are independent of the participant's behavior.

Method

Participants and Procedures

Participants were 96 adults between the ages of 18 and 58 years ($M = 34.26$, $SD = 9.95$) diagnosed with major depressive disorder (MDD).[1] The sample was largely composed of women ($n = 71$, 74%) relative to men ($n = 25$, 26%). Most individuals were single ($n = 56$, 58.3%), with 32 (33.4%) married or living with a domestic partner and 6 (6.2%) separated, widowed, or divorced. Ethnicity was primarily Caucasian ($n = 48$, 50%), followed by Asian ($n = 40$, 41.7%), African American ($n = 4$, 4.2%), Latino or Hispanic ($n = 2$, 2.1%), and other ($n = 1$, 1%). The sample was generally well-educated, with 46.6% ($n = 41$) having completed

[1] Sample sizes vary within demographic categories because of differences in missing data.

college (and no advanced studies), 33% ($n = 29$) reporting graduate or professional education beyond college, and 20% ($n = 18$) reporting some college or less. Finally, the sample was varied with respect to annual income, with 15.6% ($n = 15$) earning under $10,000, 14.6% ($n = 14$) earning between $10,000 and $25,000, 24% ($n = 23$) earning between $25,000 and $50,000, 17.7% ($n = 17$) earning between $50,000 and $75,000, and 18.8% ($n = 18$) earning more than $75,000.

Individuals were recruited through advertisements and flyers and through referrals from two outpatient psychiatry clinics at Stanford University. The vast majority of participants were self-referred (i.e., from advertisements and flyers), and half were receiving treatment (46 reporting receiving treatment, 46 reporting not receiving treatment).

All participants were initially screened by telephone to recruit individuals with a high likelihood of current depression with a relatively recent onset of the disorder (98% of the sample had had an onset within 2.5 years). Individuals who appeared to be eligible for the study were invited for an appointment at the Department of Psychology at Stanford University, where they were administered a diagnostic interview and completed self-report questionnaires. Participants who met formal criteria for study inclusion (see below) were requested to return to the laboratory approximately 1 week later to complete additional measures. Once these two sessions had been successfully completed, participants were invited for a third session to complete the life stress interview. All participants were paid $25 per hour.

All participants were interviewed with the Structured Clinical Interview for *DSM–IV* Axis I Disorders (SCID-I; First, Spitzer, Gibbon, & Williams, 1996) and met criteria for current MDD according to the *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition (*DSM–IV*; American Psychiatric Association, 1994). These individuals were screened to exclude current comorbid panic disorder and social phobia, as well as to exclude lifetime history of mania, hypomania, or primary psychotic symptoms. Participants were also excluded if they had a recent history (in the past 6 months) of alcohol or psychoactive substance abuse or dependence, and they were required to have no history of brain injury or mental retardation. Interviewers were advanced psychology graduate students and postbaccalaureate research assistants. To assess diagnostic interrater reliability for the overall project, an independent trained rater who was unaware of group membership evaluated 15 randomly selected audiotapes of SCID-I interviews. These interviews were drawn from individuals who did and did not meet study criteria, and they included people who met criteria for depression, social phobia, or panic disorder and those who did not meet diagnostic criteria. In all 15 cases, diagnostic decisions made by the independent rater matched the diagnostic decision made by the original interviewer, $\kappa = 1.00$. Although this represents excellent reliability, we should note that the interviewers used the skip out strategy of the SCID-I, which may have reduced the opportunities for the independent raters to disagree with the diagnoses (Gotlib, Kasch, et al., 2004; Gotlib, Krasnoperova, Yue, & Joorman, 2004).

Measures

History of depression. History of depressive episodes was assessed as part of the SCID-I interview, with interviewers probing the reported number of prior depressive experiences to determine whether the participant met criteria for a past episode of MDD. The frequency of total lifetime depressive episodes (including the index episode) ranged from 1 ($n = 18$) to "too many to count" ($n = 15$). The majority of participants had 4 or fewer lifetime episodes, and there were sufficient participants with up to 5 lifetime episodes within each of these categories to allow for more detailed analysis. Beyond 5 lifetime episodes, however, the number of participants per specific number of past depressive episodes decreased; consequently, for individuals with more than 5 episodes, we collapsed across episode history categories. Specifically, to provide a more uniform index of depression history and to provide for approximately equal numbers of individuals per category, individuals who reported 6 or more lifetime episodes were collapsed into three categories of lifetime history (6–10 episodes, 11–36 episodes, >36 episodes or "too many to count"; see Table 1).

Global functioning. The Global Assessment of Functioning Scale (GAF, Axis V, *DSM–IV*; American Psychiatric Association, 1994) was used to assess global functioning. The GAF is a single-rating scale used to evaluate an individual's overall level of psychological, social, and occupational functioning. Ratings are made on the basis of the SCID-I interview and range from 1 (*lowest level of functioning*) to 100 (*highest level of functioning*). The reliability of the GAF has been demonstrated in prior work (Endicott, Spitzer, Fleiss, & Cohen, 1976) and with this team of interviewers (Kasch, Rottenberg, Arnow, & Gotlib, 2002; Rottenberg, Kasch, Gross, & Gotlib, 2002).

Life-stress assessment. The Life Events and Difficulties Schedule (LEDS; Brown & Harris, 1978) was used to assess and operationalize life stress. The LEDS system employs a semistructured interview that systematically covers life domains and provides the respondent with numerous probes and opportunities to stimulate recall of past experiences. This information is subsequently presented to a panel of raters trained in the LEDS proce-

Table 1
Categorization of Participants by Past History of Major Depressive Episodes

	Total depressive episodes							
Variable	1	2	3	4	5	6–10	11–36	> 36[a]
Depression history category	1	2	3	4	5	6	7	8
Frequency	18	13	13	7	9	11	10	15
% of sample	18.8	13.5	13.5	7.3	9.4	11.5	10.4	15.6

Note. Total depressive episodes includes the index, or current, episode of major depressive disorder.
[a] Participants with more than 36 lifetime episodes generally reported they had "too many to count."

dures to (a) define life events and difficulties and (b) rate dimensions of these two forms of life stress (Brown & Harris, 1978).[2] Relevant information pertaining to stressors is presented first, with raters permitted to ask clarifying questions. Subsequently, each rater provides his or her ratings of the major stress dimensions (see below). All discrepancies are then resolved through group discussion and consensus ratings.

For all of these operations, the LEDS manuals were available to provide anchoring examples and to assist with standardization (e.g., the 520-page manual contains thousands of case vignettes to assist in defining events and assigning threat ratings). Raters were blind to information about the person's subjective response to stressors, clinical status, and other important clinical considerations and dependent variables (e.g., timing of depression onset, lifetime history of episodes). All life events that were direct consequences of depression are excluded from the analyses (e.g., work or relationship problems due to poor concentration, fatigue, irritability). (In practice, once the blind for onset date is broken, we find essentially all such events to postdate formal onset of the episode.) For secondary analyses, life events were also rated as *independent* (events that occurred entirely independently of the participant's behavior) and *possibly dependent* (events that could possibly be the result of the participant's behavior but that were clearly not due to depression).[3]

Previous research with the LEDS has established severe acute events and severe chronic difficulties as the two types of life stress most relevant for predicting the onset of depression (Brown & Harris, 1989; Monroe & Hadjiyannakis, 2002). These are explicitly defined categories of events and difficulties that are based on a high degree of contextual threat, unpleasantness associated with the situation, and a high likelihood of prolonged consequences.[4] Within the LEDS rating system, all events are rated based on extensive information about the circumstances surrounding the event and on the particular individual's biographic circumstances (i.e., contextual ratings; see Brown & Harris, 1978, 1989). Thus, there is no universal assignment of scores based on summary descriptions of the events. Nonetheless, examples are useful for understanding the general types of events typically included in the severe categories used in the present study. Examples of severe events include several terminations of core relationships, a broken engagement, and a very serious fight with a spouse. Examples of severe difficulties include highly negative marital relationships (e.g., constant serious arguing, infidelity, threats of divorce, physical abuse), impoverished economic circumstances (e.g., cannot pay bills, evicted or possessions repossessed), serious ongoing problems with children, and highly problematic work situations. Presence or absence of (a) severe acute events occurring within 26 weeks prior to the onset of a depressive episode and of (b) severe nonhealth difficulties lasting at least 2 years prior to onset represent standard procedures for operationalizing life stress within the LEDS system (Brown & Harris, 1978, 1989).[5] These were the two indicators of recent major life stress used in the analyses.

After completing the LEDS assessment by trained personnel at Stanford, the interviewer presented the detailed life-stress information via teleconferencing to trained raters at the University of Oregon (Eugene). These teleconference rating sessions occurred within a few days of the LEDS interview. The raters at the University of Oregon performed all ratings after discussion and consensus agreement and were blind to relevant dependent measures (e.g., timing of depression onset, patient emotional response to event, history of depression). On average, the interviews and rating sessions each required approximately 2 hr to complete.

The LEDS has established psychometric validity and is widely regarded as a state-of-the-art instrument for measuring life stress (Brown, 1989; Hammen, 2005). Reliability for the present project for pair-wise comparisons ranged from .72 to .79 (M = .76; Cohen's κ, corrected for differences in the number of raters per event; Uebersax, 1982). Prior research on life stress using the LEDS also indicates that life events and difficulties can be reliably assessed for at least 2 years prior to interview, with high reliability for severe events established for up to 10 years (Brown, 1989; Neilson, Brown, & Marmot, 1989).

Analyses

Preliminary analyses were conducted on major demographic and clinical variables to ensure that findings for the primary study hypotheses could not be attributed to or importantly influenced by these factors. Next, to provide an initial comparison with the existing literature, we conducted two chi-square analyses for the presence or absence of the two stress indicators (i.e., severe events, severe difficulties) for participants experiencing a first lifetime episode versus those experiencing a recurrence of depression (i.e., collapsed across number of recurrences). Hierarchical regression analyses were then conducted to predict variation in full depression history, with the presence or absence of severe difficulties entered first (owing to temporal precedence of difficulties being present for a minimum of 2 years) and the presence or absence of a severe event in the past 26 weeks entered second.[6] To test for the homogeneity of the regression lines and to rule out any interaction between difficulties and events, we entered the cross-product interaction term into the equation last (Cohen & Cohen, 1983). Finally, secondary analyses were conducted to control for the relevant demographic and clinical variables and to examine inde-

[2] Raters were trained by Scott M. Monroe, who was trained in the LEDS procedures by Tirril Harris. The number of raters per case ranged from one to four, with the majority involving at least three or four raters. Scott M. Monroe was one of the raters for 99% of the rating sessions.

[3] Although in theory severe difficulties could be divided into independent and possibly dependent categories, in practice such stressors are almost always possibly dependent. This is due to the fact that there is a 2-year duration requirement for severe difficulties, which makes it very hard to eliminate the possibility that the participant's behavior to some degree influences this chronic form of stress.

[4] Specifically, severe events are defined as events rated 1 on long-term threat or 2a on long-term threat and subject or joint focused. All event ratings were made contextually and consensually. Severe difficulties are defined as difficulties rated 1 to 3 (on a 6-point scale) that began 2 or more years from the onset of the current episode and did not involve primarily a health difficulty. See Brown (1989) for further details on these well-standardized rating procedures.

[5] Prior work has established the presence or absence of severe events as the most important predictor of depression onset (as opposed to a cumulative measure including all severe events; Brown & Harris, 1978, 1989; Monroe & Hadjiyannakis, 2002).

[6] Comparative analyses using either 6- or 12-week intervals for assessing severe events produced similar findings. In fact, all severe events occurred within an 18-week time frame, with the vast majority occurring within about 14 weeks.

Table 2
Hierarchical Regression Model for Severe Life Events and Severe Difficulties Predicting Lifetime History of Depressive Episodes

Stressor type	*B*	Multiple *R*	R^2	ΔR^2	ΔF (*df*s)	*p*
Step 1: Severe difficulty (present/absent)	.255	.255	.065	.065	6.56 (1, 95)	.012
Step 2: Severe event (present/absent)	−.339	.424	.180	.115	13.01 (1, 94)	.001
Step 3: Severe Event × Difficulty interaction	.113	.434	.189	.009	0.98 (1, 93)	.325

Note. Severe difficulties were present for at least 2 years prior to onset of the index depressive episode, and severe events occurred within a 26-week period prior to the onset of the index depressive episode.

pendent and possibly dependent severe events in relation to lifetime history of MDD.

Results

Preliminary Analyses

The major demographic variables, including sex, marital status, ethnicity, and income, were unrelated to the presence or absence of a severe life event or a severe chronic difficulty. Participant age, however, was related to chronic difficulties, with older participants more likely to have a severe chronic difficulty: participants with a severe difficulty, $M = 43.57$, $SD = 9.96$; participants without a severe difficulty, $M = 33.46$, $SD = 9.59$, $t(87) = 2.69$, $p < .005$.

The major clinical variables, including intake-symptoms severity (coded symptoms from the SCID-I), GAF, and episode length at intake, were tested for associations with severe events, severe difficulties, and depression history. Severe events were related to global functioning: participants with severe events, $M = 50.68$, $SD = 8.03$; participants without severe events, $M = 54.48$, $SD = 7.42$, $t(94) = 2.16$, $p < .04$. Age was significantly correlated with history of depressive episodes ($r = .27$, $p \leq .02$), with older participants having a higher likelihood of reporting more previous episodes of depression.[7] Consequently, the secondary analyses reported below control for the influences of age and GAF scores.

Primary Analyses

The presence of a severe event was significantly related to the participant experiencing a first lifetime depressive episode: 50% (9 of 18) of first-onset cases reported a severe event, compared with 21% (16 of 78) of all combined recurrence cases, $\chi^2(1, N = 96) = 6.60$, $p \leq .01$. Although not statistically significant, the reverse pattern of association was found with respect to severe difficulties: No (0 of 18) first-onset cases reported a severe difficulty, compared with 9% (7 of 78) of all recurrence cases, $\chi^2(1, N = 96) = 1.74$, $p > .15$.

In testing the two types of severe life stress together in a regression model predicting full depression history, we found severe difficulties to be significantly related to a greater history of prior depressive episodes ($p < .02$). Severe events, entered in the second step of the hierarchical regression, also significantly predicted depression history ($p < .001$). For acute events, however, the association was the reverse of that for chronic stressors: The presence of a severe event was significantly more likely for individuals with fewer prior episodes of depression (see Table 2). The descriptive data for severe events and severe difficulties, stratified by lifetime episodes of depression, are presented in Table 3.

Secondary Analyses

Secondary analyses were conducted to control for the demographic and clinical correlates and to examine possible differences in effects for independent and possibly dependent severe life events. First, with regard to demographic (age) and clinical (GAF) variables that were found to be significantly related to the independent and dependent variables (see the *Preliminary Analyses* section above), separate analyses controlling for the effects of these variables did not alter the basic pattern or the level of statistical significance of the primary findings. Both severe difficulties, $\Delta F(1, 85) = 3.96$, $p \leq .05$, and severe events, $\Delta F(1, 84) = 13.07$, $p \leq .001$, continued to significantly predict depression history. Thus, the differential relations found for severe events and severe difficulties with regard to history of depressive episodes cannot be explained by demographic or clinical correlates.

Second, we compared participants with severe independent events ($n = 7$) and participants with severe possibly dependent events ($n = 18$) with respect to depression history. Severe independent events were not significantly associated with history of a first lifetime onset versus a recurrence: 6% (1 of 18) of first-onset cases reported a severe independent event, compared with 8% (6 of 78) of all combined recurrence cases, $\chi^2(1, N = 96) = 0.75$, $p > .75$. In contrast, the presence of a severe possibly dependent event was significantly related to a first lifetime depressive episode: 44% (8 of 18) of first-onset cases reported a severe possibly dependent event, compared with 13% (10 of 78) of all combined recurrence cases, $\chi^2(1, N = 96) = 9.60$, $p \leq .002$. Finally, we modeled severe

[7] Although participants with first lifetime episodes did not differ from participants with one or more recurrences in terms of length of the index episode ($M = 8.02$, $SD = 10.81$, and $M = 7.14$, $SD = 6.40$, respectively), there was a significant correlation when total depression history was correlated with length of the index episode ($r = -.21$, $p < .05$). This association indicated that participants with a greater number of prior episodes had a relatively briefer duration of the index episode. Controlling for current episode length did not diminish the pattern or statistical significance of the major findings. Indeed, if there was a problem with confounding between recall period and reporting of events, one would expect it to operate against our finding of major events predicting fewer lifetime episodes (i.e., the participants with a greater history would have the shorter recall period and would be likely to report more events).

Table 3
Categorization of Depression History and Frequencies and Percentages of Participants per Category

	Lifetime history of depressive episodes							
Type of severe stress and category	1	2	3	4	5	6–10	11–36	> 36[a]
Event								
n	9	5	3	2	2	3	0	1
%	50	38.5	23.1	28.6	22.2	27.3	0	6.7
Difficulty								
n	0	0	0	1	1	1	1	3
%	0	0	0	14.3	11.1	9.1	10.0	20.0
Total	18	13	13	7	9	11	10	15
Depression history category	1	2	3	4	5	6	7	8

Note. Life time history of depressive episodes includes the index, or current, episode of major depressive disorder.
[a] Participants with more than 36 lifetime episodes generally reported they had "too many to count".

difficulties, severe independent events, and severe possibly dependent events in a hierarchical regression analysis predicting lifetime depression history. As expected from the prior analysis, severe difficulties entered on the first step were significantly related to a greater history of depressive episodes ($p < .02$). In contrast, severe independent events entered on the second step were not a significant predictor of depression history, $\Delta F(1, 93) = 1.58$, $p > .20$. In the last step of the regression equations, severe possibly dependent events continued to significantly predict less of a depression history, $\Delta F(1, 92) = 11.33$, $p < .001$. Severe possibly dependent life events appear to be the acute stressors of particular relevance for the association between life events and lifetime history of depression.

Discussion

There has been extensive discussion and research on the associations among life stress, depression, and recurrence of the disorder. Although the results of a number of studies underscore the importance of severe life events for first lifetime episodes relative to recurrences, few investigators have pursued this issue by examining the prevalence of major life events over specific recurrences (e.g., first, second, third). Not only did the present study examine major life events in relation to such a differentiated history of depression, but further, it is one of the few investigations to also examine chronic stress to understand differences between first lifetime episodes of depression and recurrences with respect to life stress. Our results establish the independent association of both forms of severe stress with the onset of a depressive episode and suggest that each form of stress plays a different role with regard to the lifetime history of depression.

As predicted for acute life events, severe events are significantly more likely to precede a first lifetime episode than all recurrences combined. This finding is reinforced and expanded when recurrences are classified more specifically by episode number. The changing association between severe events and recurrence persists well past a first lifetime recurrence (see Table 3). These data are consistent with the premise that severe events continue to be of etiological importance well after the first lifetime episode but that such events become a less common contributor to recurrence for participants with a greater history of depression. Indeed, if the etiologic effects of severe events remain germane for individuals with up to three lifetime episodes of depression, then severe events are of causal significance for the majority of people estimated to suffer from MDD in the general population (American Psychiatric Association, 1994; Monroe & Harkness, 2005). As other causal arrangements or pathways become more influential in the etiological picture with repeated recurrences, they may increasingly supplant, but not completely replace, the causal influence of major events. This process suggests that with repeated recurrences, there will be diminishing statistical power in traditional research designs for detecting the impact of the increasingly infrequent major events. Investigators will need to target the question of impact more specifically, examining the likelihood of recurrence given the occurrence of a major event as a function of depression history (see Monroe & Harkness, 2005).

Although previous work has shown that chronic difficulties are associated with the onset of depression (Brown & Harris, 1978), there has been a paucity of research on this topic, especially compared with the extensive research on major life events (Hammen, 2005). Few studies have examined chronic difficulties in relation to first episode versus recurrence considerations (cf. Daley et al., 2000). The present findings suggest that major difficulties are a relatively small factor in accounting for episode onset overall (given the relatively low incidence of severe difficulties in the full sample, 7.3%). Yet the pattern of these data is intriguing. On the one hand, these findings suggest that major difficulties are not of great importance for people with one or with just a few lifetime episodes. If this proves to be the case, it would help to direct and sharpen the focus on acute major events in relation to the majority of episodes of depression in the population at large. On the other hand, people with multiple episodes of depression are among the most vulnerable and impaired, requiring special attention to arrest the continued progression of pathology in their lives. Severe chronic difficulties may be a large factor in bringing about such especially frequent recurrences and may provide an important focus for intervention. In this light, understanding how severe difficulties originate and how they may contribute to the recurrence of depression would be useful research avenues to pursue.

These findings for major events and major difficulties together help address the question of what changes over successive recurrences with respect to life stress. The design of the present study does not permit a direct test of causal premises (i.e., currently nondepressed persons with and without a history of depression were not assessed in the present study). And as noted above, future work will need to address whether, in addition to the changing frequency of events as a function of depression history, there is a diminishing impact of such stressors for triggering depression. Nevertheless, it is in this context of understanding possible changes in impact of life stress over time that the present findings for severe events and difficulties are of particular interest. In contrast to the decreasing association demonstrated for severe life events, severe chronic difficulties were more common for individuals with many prior depressive episodes. (Indeed, not a single person with fewer than three lifetime episodes reported a severe difficulty.) Such results suggest one possible mechanism through which the role of life stress may change over repeated recurrences: The overall contribution of severe events may lessen, whereas the emerging contribution of severe difficulties may increase.

The greater prevalence of severe difficulties as lifetime history of depression increases is consonant, too, with the stress-generation hypothesis (Hammen, 1991, 2005). For instance, it might be expected that with many lifetime episodes, adversities accrue and become more enduring. As these chronic stressors become major problems in themselves, they likely spawn additional adverse life events. Such processes involving the generation of both chronic and acute events would clearly increase the total stress in the lives of people who suffer from recurrent depression. The question then arises as to the potential of varied types and severities of stressors for precipitating recurrences of depression (i.e., many types of life stress may be undesirable and psychologically noxious but not necessarily capable of triggering clinical depression; Harkness et al., 1999; Monroe & Simons, 1991). Although the stress-sensitization model and stress-generation model can be viewed as providing alternative explanations of the increasing likelihood of recurrence with repeated depressive episodes, these two models can also be viewed as mutually reinforcing. That is, as repeated depressions lead to increasing stress (stress generation), and as lesser severities of stress acquire the capability of triggering recurrence (stress sensitization), these two processes combine to render the person with recurrent depression especially susceptible to another episode.

Given the potential importance of both stress generation and stress sensitization, it is useful to speculate about such matters from the present data. In this vein, it is interesting to consider that the increased incidence of severe difficulties in the highly recurrent group reflects the continued potential of major stress to initiate new episodes of depression. This interpretation reinforces the idea that it is change in the frequency, rather than in the impact, of severe events that accounts for the lower prevalence of severe events prior to recurrence as lifetime history of depression increases. Although such inferences are consistent with the present data, they are not based on strong tests of the hypotheses. Future work that includes life events and difficulties of differing severity levels is needed to provide more definitive evidence of the mechanisms through which severe events may be replaced in triggering the recurrence of depression and how the stress-generation and stress-sensitization models may play out with respect to one another over time (Hammen, 2005; Monroe & Harkness, 2005).

Comparisons with other studies are limited, given the lack of detailed information in other studies on major stress and the onset of depression over successive lifetime episodes. With regard to acute major events, Kendler, Thornton, and Gardner (2000) found the odds ratio between a major event and depression onset to decrease progressively from a first lifetime episode over successive recurrences. They noted that the association continued to decrease up to nine episodes. Although Kendler et al.'s findings are important for documenting the general changes between major events and onset as a function of depression history, they do not illuminate the possible underlying mechanisms. As we have indicated, it is not clear whether such findings are accounted for by a change in frequency or by a change in impact of major events. The present results provide a useful complement to Kendler et al.'s data, revealing that the diminishing frequency of major events with increasing lifetime history of depression is an important factor for understanding the overall changing association between major stress and recurrence over time. These data again lend some, albeit limited, support to the stress sensitization premise. For example, if we had found a constant rate of severe events for people with progressively more lifetime episodes, it would suggest that Kendler et al.'s findings were due to a diminishing impact of major events over successive recurrences. Again, future work will need to target the frequency and impact considerations more directly (Monroe & Harkness, 2005).

Only one other study has addressed the association of major chronic difficulties with regard to the distinction between first lifetime onsets and recurrences. Daley et al. (2000) found history of previous depression to interact with chronic stress. For women without a history of previous depression, chronic stress significantly predicted a first lifetime onset of depression over a 5-year period. In contrast, for women with a history of previous depression, chronic difficulties did not predict a new recurrence. Although these data appear to be inconsistent with the present findings, it is important to consider differences between these two studies in their designs and methods. With respect to design, the present study focused on major stress in relation to a differentiated recurrence history of depressed persons. The most direct comparison of the present study with Daley et al.'s report involves the chronic stress means for women experiencing a first lifetime onset of depression ($M = 14.50$, $SD = 2.01$) versus women experiencing any recurrence of depression ($M = 14.06$, $SD = 2.53$). Thus, although chronic difficulties differentially predicted a first lifetime episode of depression in Daley et al.'s study, chronic difficulties did not appear to diminish appreciably for recurrences overall.[8] Moreover, given that Daley et al.'s sample was composed of relatively young women (mean age = 18.29 years at study entry),

[8] Mean chronic stress for the women without a history of depression and without an episode over the 5-year follow-up period was 12.30 ($SD = 2.00$), whereas average chronic stress for women with a history of depression without a recurrence over the follow-up period was 13.50 ($SD = 2.81$). Thus, it does not appear that there were significant differences in mean levels of chronic stress between women who were experiencing a first onset of depression and women who were experiencing a recurrence of depression in Daley et al.'s (2000) study.

it is unlikely that there were many people with an extensive history of recurrences, the very people who evidenced a higher incidence of severe difficulties in the present study. Thus, without more differentiated information about past history of depression, and with such a relatively young sample, it is difficult to derive firm conclusions regarding comparisons with the present study.

Appreciating the differences in the methods used in the two studies may also be informative for future work. Chronic difficulties in Daley et al.'s (2000) study were represented by a total chronic stress score, summed across five life domains for the 3-month period prior to onset (and a matched period for controls). In the present study, chronic stress was represented by the presence or absence of a severe difficulty (which is defined by high threat and lasting a minimum duration of 2 years prior to depression onset; Brown & Harris, 1978). Thus, the two studies differed in terms of severity and duration requirements for the chronic stress indicators. Given the 3-month time frame of Daley et al.'s investigation for defining chronic stress, it is likely that their measure included more recent and acute stress features than did our measure, which, in turn, could help to explain the differential association with first onset versus recurrence. At the present stage of knowledge, it is premature to judge which approach is more valid or useful. Clearly, more studies using similar high quality measures need to take into account the potential importance of chronic difficulties for depression onset and recurrence (Hammen, 2005).

Secondary analyses on independent and possibly dependent events indicate that it was largely the latter category that was significant with regard to lifetime history of depression. This might be in part due to the greater frequency of possibly dependent events in general (and in the present sample, 7 independent severe events vs. 18 possibly dependent severe events). It is important to note, however, that further analysis suggests that, once independent severe events were controlled for statistically, the effects for possibly dependent events on history of depression remained significant and strong. It is also noteworthy that other research has found the independent (or "fateful") events to be especially strong for predicting depression in general (i.e., for first onsets and recurrences; Shrout et al., 1989). It may be that events that are in part related to the behavior of the person are especially pertinent for first lifetime episodes of depression. Finally, we also investigated the interaction between severe events and severe difficulties. There was no indication that either form of stress operated in a manner conditional upon the other. Consequently, it appears that each form of severe stress is significant and independent in its relations to depression history.

The strengths of the present study include a well-characterized sample that is informative for a wide range of reported prior depressions. The assessment of life stress was based on one of the most reliable and valid systems available and included rigorous assessment of both major life events and major ongoing difficulties. Study inclusion criteria ensured a sample of individuals with a relatively recent and clear onset of a depressive episode (i.e., participants were relatively free of symptoms and had no depressive episode for 6 months prior to the index episode, thereby ensuring the sample was not confounded with chronic depression). These results provide important statistical and descriptive information for better understanding the relation between severe events and difficulties with regard to the onset of depression over successive recurrences. To test causal processes more directly, future researchers will need to include currently nondepressed persons, especially nondepressed persons with varied histories of total lifetime depressive episodes.

In addition, it is important to note that the present work, and the vast majority of the work in the literature, is based on a between-subjects analysis of life stress and recurrence. That is, associations for life stress in relation to differing histories of MDD are based on different groups of individuals with different histories of MDD. The design of the present study does not permit one to rule out the possibility that something about the different groups, and not necessarily changes in relation to stress over successive recurrences, is of relevance with regard to stress. Ideally, future research will also include a longitudinal within-subject component to test the changing association between life stress and recurrence over repeated episodes for the same individuals (see Kendler et al., 2000). To justify the intensive research demands that accompany such longitudinal research, however, a firm foundation of supportive empirical evidence needs to be assembled. The present findings represent an important contribution toward this goal.

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