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The Relationship Between Stress and Depression in First Onsets Versus Recurrences

A Dissertation Presented

by

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Abstract of the dissertation

The Relationship Between Stress and Depression in First Onsets Versus Recurrences

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Overall, research has evidenced support for Post's model (1992) which asserts that the first episode of depression is more likely to be associated with severe life events than subsequent episodes. In spite of this, there are significant gaps in our understanding of the stress-depression association. This study aimed to address four gaps: (1) identify the explanatory model underlying the association (stress sensitization versus stress autonomy); (2) elucidate how the role of stress changes with successive episodes; (3) reveal the role of non-severe events; and (4) examine the influence of comorbid anxiety. To address the first 3 gaps, I tested the two models proposed to explain how the stress-depression association changes over the course of depression. To do so, I examined the impact and occurrence of severe events and non-severe events in a 5-year longitudinal sample of late-adolescent women using cross-sectional and longitudinal analyses. Overall, I found support for the stress sensitization model over the stress autonomy model. Specifically, the occurrence of dependent, but not independent, severe events was greater for first onsets than recurrences using both cross-sectional and longitudinal analyses. In

addition, the impact of independent, but not dependent, severe and non-severe events was greater in individuals with a history of depression cross-sectionally, but not longitudinally. To examine the influence of comorbid anxiety, I repeated the cross-sectional and longitudinal analyses for those with and without a lifetime history of anxiety disorders. Results revealed changes in the impact and occurrence of some, but not all, events as a function of lifetime history of anxiety disorders. The results were discussed in terms of the underlying mechanisms of the stress-depression association and future directions of research were elaborated.

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## INTRODUCTION

The nature of the stress-depression relationship in first onsets versus recurrences has been of great interest to depression researchers. Central to this issue is Post's (1992) assertion that the nature of the relation between severe life events (SLEs) and depression changes over time, such that SLEs are more likely to be associated with first than subsequent episodes of depression. Indeed, all major reviews on the topic (Mazure, 1998; Monroe & Harkness, 2005; Stroud, Davila & Moyer, 2008) have evidenced at least some support for Post's assertion.

However, despite this consistency, there remain significant gaps in our understanding of the stress-depression relationship, particularly with regards to: (1) the explanatory model underlying this association (stress sensitization vs. stress-autonomy); (2) the changing role of life stress over time; (3) the role of events of lower severity (LLEs; 4); and (4) the influence of comorbid anxiety on the association.

### The Explanatory Model Underlying the Stress-Depression Association

There are two theoretical models proposed to explain the association between SLEs and depression in first onsets and recurrences: (1) the stress autonomy model (SA), which suggests that episodes of depression begin to occur autonomously of stress with repeated episodes, and (2) the stress sensitization model (SS), which suggests that events of lower and lower severity (i.e., LLEs) trigger episodes with successive recurrences. Indeed, Post and his colleagues discuss "kindling" and "sensitization" as "two distinct paradigms" based on "two very different models" of "electrophysiological kindling" (SA) and "behavioral sensitization" (SA) respectively (e.g., Post & Weiss, 1998; p. 193). However, most research has not recognized the opposing meanings of these models, and instead

refers to Post's model or the kindling model as a singular unit (Hlastala et al., 2000; Monroe & Harkness, 2005). As a consequence, the same findings may be interpreted as either supporting or not supporting the model, depending on whether the interpretation is based on an autonomy or sensitization perspective (Hlastala et al., 2000). For example, the decline in the strength of the association between severe life stress and depression across episodes evidenced in recent studies (e.g., Kendler, Thornton & Gardner, 2000) can be explained by both models. From the perspective of the SS model, the decline is interpreted to suggest that SLEs are less likely to trigger episodes over time because individuals become sensitized to stress, such that events of lower severity (LLEs) develop the capacity to trigger episodes of depression (Monroe & Harkness, 2005). Alternatively, from the perspective of the SA model, the decline in the strength of the association is interpreted to suggest that SLEs are less likely to precipitate episodes over time because episodes begin to occur independently of stress with successive recurrences (Monroe & Harkness, 2005).

Thus, the decline in strength of the stress-depression association found in recent studies is consistent with both the SS and SA models, as Monroe and Harkness (2005) have pointed out. To distinguish the models, it is necessary to investigate if episodes are triggered by increasingly less severe events (consistent with the SS model) or if episodes arise independently of stress (consistent with the SA model). To do so, the role of stress in terms of impact and occurrence (called frequency by Monroe & Harkness in their review) must be examined for SLEs and LLEs separately, as we discuss below.

The Changing Role of Stress over Time in the Stress-Depression Association

As Monroe and Harkness (2005) have pointed out, most existing research is ambiguous with regard to the changing role of life stress across the course of disorder. That is, existing research does not reveal whether there is a decline in the impact of SLEs on depression (i.e., SLEs become less and less capable of triggering depression, losing their potency to trigger episodes) or a decline in the occurrence of SLEs prior to depression (i.e., SLEs are less and less likely to be present prior to episodes as LLEs are more and more common [SS model] or episodes arise independently of stress [SA model]) or a decline in both impact and occurrence. Without investigating changes in the impact and occurrence of life stress, the stress-depression relationship cannot be understood and the two models cannot be differentially tested (Monroe & Harkness, 2005).

In terms of the impact of SLEs, one of the distinctions between the SS and SA models is whether or not SLEs lose the capacity to trigger episodes. As summarized in Table 1, the SS model predicts that SLEs increase in impact (as the individual is sensitized to stress), whereas the SA model predicts that SLEs decrease in impact (stress loses the capacity to trigger episodes as new processes develop that trigger episodes independently; Monroe & Harkness, 2005).

In terms of the occurrence of SLEs, both the SS and SA models predict that the occurrence of SLEs prior to episodes will decrease across the course of the disorder. In the SS model, the occurrence of SLEs decreases, as the occurrence of LLEs increases: that is, increasingly lower level events (rather than SLEs) precipitate episodes as the individual becomes sensitized to stress. In the SA model, the occurrence of SLEs prior to depression diminishes, as episodes become more and more independent of life events,

and less likely to be triggered by life events. Thus, both models predict a decrease in the occurrence of SLEs as triggers of recurrences, but for theoretically different reasons (Monroe & Harkness, 2005). Thus, to distinguish the models, the impact and occurrence of SLEs and LLEs need to be examined separately.

#### The Role of Events of Lower Severity in the Stress-Depression Association

Although most research has focused on SLEs (e.g., end of core relationship [Monroe et al., 2006], job loss), some has documented the role of LLEs (e.g., end of part-time job, moving; Monroe et al., 2006) in triggering episodes of depression. Research has documented the role of lower stress life events or lower level total stress in predicting episodes in adolescents and adults with a history of childhood adversity (Espejo et al., 2006; Hammen, Henry & Daley, 2000; Harkness, Bruce & Lumley, 2006; Rudolph & Flynn, 2008). Several studies have shown that LLEs (all rated by the Life Events and Difficulties Schedule; Brown & Harris, 1978, 1989) predicted recurrences (Harkness & Monroe, 2006; Lenze, Cyranowski, Thompson, Anderson & Frank, 2008; Monroe Roberts, Kupfer & Frank, 1996; Monroe et al., 2006, Ormel, Oldehinkel & Brilman, 2001). Thus, research supports the role of LLEs in depression and in predicting recurrences specifically.

Because the SS and SA models make contrasting predictions for the role of LLEs (illustrated in Table 1), investigating the role of LLEs can distinguish between the models. From the SS perspective, the impact of LLEs increases across the disorder, as individuals become sensitized to stress over time, lowering the threshold of stress needed to trigger a recurrence. As well, the occurrence of LLEs prior to episodes increases: LLEs become more and more likely to be present prior to episodes as individuals become sensitized to



stress over time, allowing LLEs to become increasingly likely to trigger episodes (i.e., the impact of LLEs increases). In contrast, from the SA perspective, the impact of LLEs decreases across the disorder, as episodes become more autonomous and occur via other biological mechanisms (as elaborated by Monroe and Harkness [2005] there will be an initial increase in impact followed by a decrease as the mechanisms emerge). Likewise, the occurrence of LLEs prior to episodes decreases as episodes are increasingly independent of stress; it becomes less likely that LLEs are triggers. Thus, the SS and SA models make contrasting predictions about the role of LLEs, allowing an investigation of these events to ascertain the underlying mechanisms of the stress-depression association (Monroe & Harkness, 2005). Research on LLEs (Harkness & Monroe, 2006; Lenze et al., 2008; Monroe et al., 1996; Monroe et al., 2006, Ormel et al., 2001) seems to support the SS model, as LLEs predict recurrences, yet there has not been a direct test of the models and some existing research is limited by the use of highly recurrent patient samples, where stress processes may be difficult to detect and which may not generalize to those with fewer lifetime episodes (Monroe & Harkness, 2005; Monroe et al., 2006).

#### The Influence of Comorbid Anxiety on the Stress-Depression Association

Depression and anxiety are highly comorbid (e.g. Kessler et al., 1994), and cases of pure depressive disorder are uncommon (Alloy Kelly, Mineka, & Clements, 1990). As such, ignoring the effect of comorbidity may obscure results of research on depression, as associations may be linked to comorbid depression and not depression alone (Bruce et al., 2005). Therefore, an examination of the effect of comorbid anxiety on Post's model is imperative, as several lines of evidence predict that anxiety will affect the stress-depression association.

First, considerable literature documents the negative impact of comorbid anxiety on the course of depression. One of the most consistent findings is that comorbid anxiety slows recovery of major depressive episodes (e.g., O’Leary, Costello, Gormley, & Webb, 2000), with estimates indicating that the duration of recovery is twice as long as noncomorbid patients (Clayton et al., 1991). In addition to current comorbidity, research has shown that lifetime history of anxiety disorders delays recovery (McLeod, Kessler & Landis, 1992). Further, current comorbid anxiety (O’Leary et al., 2000), current subthreshold symptoms of anxiety (Sherbourne & Wells, 1997), and lifetime history of an anxiety disorder (AD; Giles Jarrett, Biggs, & Guzick, 1989) are all predictors of the recurrence of major depression. Notably, in a 15-year prospective study, individuals with two or more episodes of depression were distinguished from those with a single episode according to comorbid anxiety: those in the recurrent group were significantly more likely to have a lifetime history of anxiety and to have multiple lifetime ADs (Wilhelm, Wilhelm, Parker, Dewhurst-Savellis, & Asghari, 1999). Thus, current comorbidity and lifetime prevalence of ADs affects the course of depression, most importantly in terms of predicting recurrences.

Second, comorbid anxiety affects the occurrence and severity of life events. Some research suggests that individuals with co-existing anxiety and depression experience higher levels of stress. For instance, in a sample of individuals with Generalized Anxiety Disorder (GAD) and/or MDD, those with comorbid MDD and GAD exhibited higher levels of stress than those experiencing either disorder alone (Newman & Bland, 1994). In another study, the median number of precipitating events was significantly higher for patients with a comorbid AD than for those without (Leskela et al., 2004). One process

by which anxiety increases life stress is stress generation (Hammen, 1991). For example, women who had depression comorbid with another Axis I disorder (of which 58% were experiencing comorbid anxiety) experienced higher levels of dependent life stress in a 1-year follow-up even after controlling for depression severity (Daley et al., 1997).

Similarly, Harkness and Luther (2001) found that those with both comorbid anxiety and dysthymia experienced higher rates of dependent life events prior to onset of a major depressive episode (MDE). Thus, research indicates that the presence of anxiety may impact the level of life stress generated.

. Third, although less research has focused on the association between life events and ADs than life events and depression (Horesh, Amir, Kedem, Goldberger, & Kotler, 1997), a large number of studies have provided evidence for the association. For example, research has demonstrated an excess of life events in the period prior to the onset of panic disorder (for a review see Servant et al., 1991; Faravelli, Paterniti & Servu, 1997; Horesh et al., 1997; Manfro et al., 1996; Roy-Byrne, Geraci & Uhde, 1996), obsessive-compulsive disorder (OCD; deLoof, Zandbergen, Lousberg, Pols, & Griez 1989), and GAD (Barrett, 1979). Additionally, there has been a focus on differences between life events that precipitate anxiety and those that precipitate depression both theoretically (e.g., Bowlby, 1980) and empirically (e.g., Barrett, 1979). For instance, evidence suggests a tendency for loss events to be associated with depression and danger (or threat) events to be associated with anxiety (Brown, 1993; Eley & Stevenson, 2000; Finlay-Jones & Brown, 1981; Sandin, Chorot, Santed, & Valiente, 2004). Additionally, research suggests that cases of mixed anxiety-depression are likely to be preceded by both loss and danger events (Brown, 1993; Finlay-Jones & Brown, 1981). In the present

study, the association between life events and ADs is important because it allows for the possibility that these experiences may lead to the processes of sensitization (SS) and/or kindling (SA), as discussed in the following paragraphs.

Although Post's model was developed in the context of depression (Post, 1992), he indicated that loss events "may have very different cognitive, behavioral, and neurobiological consequences" than threat events (which are more likely associated with post-traumatic stress disorder; PTSD), but these syndromes likely involve some of the same "mechanisms" (p. 1004). In subsequent publications, the sensitization and/or Kindling phenomena were elaborated on in the context of several ADs including PTSD, panic disorder, social phobia and OCD (Post & Weiss, 1998; Post, Weiss & Smith, 1995). For instance, Post and colleagues linked the course of panic disorder to both Kindling (stress autonomy) and sensitization. The authors asserted that the tendency for panic attacks to be initially precipitated by environmental triggers and later occur spontaneously exhibits a Kindling (or SA) pattern; and the tendency for initial triggers to generalize to other triggers or contexts (appearing spontaneous, but not) exhibits a behavioral sensitization pattern (Post & Weiss, 1998). Thus, Post and colleagues have posited that the same processes of sensitization and kindling involved in the stress-depression relationship occur in the context of ADs.

In addition, there is recent evidence suggesting that history of AD can have a direct impact on stress sensitization. As discussed, research has documented evidence of sensitization to stress as a function of childhood adversity, demonstrating that individuals with a history of childhood adversity are more vulnerable to depression at low levels of stress (Hammen, Henry & Daley, 2000; Harkness, Bruce & Lumley, 2006; Hazel,

Hammen, Brennan & Najman, 2008; Rudolph & Flynn, 2007). Recent work suggests that this sensitization effect may be amplified by the presence of comorbid anxiety.

Specifically, youth with a history of childhood adversity showed greater severity of depressive symptoms following low levels of stress, but those with both childhood adversity and a history of anxiety disorder, showed greater depression symptom severity in response to stress (Espejo et al., 2006). Thus, research is emerging suggesting that anxiety may impact sensitization to stress, at least in youth with a history of childhood adversity.

Most individuals experiencing ADs subsequently develop depression rather than the reverse (Alloy et al., 1990). This is important because it allows for the possibility that individuals may be sensitized (or kindled) to stress prior to their first onset of depression. The idea that individuals experiencing depression could be “presensitized” or “prekindled” to stress based on lifetime comorbidity of ADs is novel, although, research has suggested that there may be multiple environmental or genetic pathways to the “sensitized” or “kindled” state (Kendler, Thornton & Gardner, 2001). For instance, research has documented sensitization to stressors as a function of childhood adversity (e.g., Hammen et al., 2000) and genetic risk (Caspi et al., 2003; Kendler et al., 2001; Kendler et al., 2000). For example one study suggested that those with high-genetic risk were presensitized or prekindled prior to the first MDE, as the decline in the strength of the stress-depression association across episodes occurred for low- but not high-genetic risk (Kendler et al., 2001). Although we cannot ascertain whether a prekindling or presensitization effect occurred (or both), this study illustrates that these processes may occur prior to the first MDE. Together, these findings lend indirect support to the

assertion that sensitization or kindling may occur prior to first onset of depression in the context of anxiety, such that individuals are “pre-sensitized” or “pre-kindled” to stress if the anxiety occurs prior to depression.

Fourth, comorbid anxiety affects the impact of life events. As discussed, sensitization lowers the threshold for the severity level of events needed to trigger an episode (Post, 1992; Post & Weiss, 1998) and therefore increases the impact of life events (Monroe & Harkness, 2005). In addition to the possibility that anxiety can advance the neurological processes of sensitization and increase the impact of life events (discussed above), there are additional reasons to predict that life events may have a greater impact for those with comorbid anxiety and depression than for those with depression alone. First, the presence of anxiety may decrease social and personal resources (Bronisch & Hecht, 1990), increasing the impact of LLEs. Second, anxiety may act as a “chronic stressor” as it may precede or persist between MDEs, amplifying the impact of stressful life events (as research suggests that long-term difficulties increase the effects of stressful life events; Ormel, Oldehinkel & Brilman, 2001), particularly when there is a match between the chronic stressor and the life event (Brown & Harris, 1989). Third, because individuals with comorbid anxiety show elevated levels of neuroticism (Weinstock & Whisman, 2006), they may experience events as more subjectively stressful, increasing their impact. This is consistent with research showing that high levels of neuroticism are associated with greater impact of stressful life events (Ormel et al., 2001). Additionally, perceived uncontrollability and past experiences of uncontrollability/helplessness occurring in the context of anxiety may function to increase feelings of helplessness in the presence of life events (Alloy et al., 1990; Mineka, Watson & Clark, 1998), leading to their increased

impact. Thus, several lines of research indirectly predict that the impact of events will be greater in those with comorbid anxiety.

To summarize, there are several reasons to predict that the presence of comorbid anxiety will influence the stress-depression relationship with successive recurrences, compelling a test of the influence of comorbid anxiety on the occurrence and impact of life events.

### The Current Study

In the present study, I investigated the impact and occurrence of SLEs and LLEs, in a 5-year longitudinal community sample of 155 young adult women, with the purpose of comparing the SS and SA models. The models were compared in a young ethnically diverse community sample, where most individuals were experiencing their first or second recurrence, alleviating concerns inherent in using samples with multiple recurrences (e.g., Monroe & Harkness, 2005) and patient samples (e.g., Paykel, 2003). As discussed, existing research examining LLEs has focused largely on patient samples (eg., Monroe et al., 2006; Monroe, Slavich, Torres & Gotlib, 2007), and because patient status may impact the stress-depression association (Stroud et al., 2008), it is important to examine the models in a community sample. In addition, interviewer-based contextual measures were used to assess life events and interviews were used to assess diagnosable depression at all time points.

In order to test the models, occurrence and impact were defined according to definitions provided by Monroe and Harkness (2005). That is, the occurrence of life events was defined as the conditional probability of a life event given an MDE whereas the impact of life events was defined as the conditional probability of an MDE given a

life event. The conditional probabilities for impact and occurrence of life events were compared for those with a history of depression to those without a history of depression in order to examine whether the impact and occurrence of life events depends on a history of depression (see Table 2).

Occurrence and impact were examined with regards to four different types of life events. As discussed, in addition to SLEs, LLEs were examined to elucidate the underlying models of the stress-depression relationship. Events were further dichotomized by independence (the extent to which the event occurs outside of the control of the individual). Thus far, some research has found independent severe events to be most potent in triggering first onsets and recurrences (Shrout et al., 1989), whereas other research calls attention to important role of dependent interpersonal events in predicting depression (e.g., Hammen, Marks, Mayol & DeMayo, 1985). Further, recent research has suggested severe independent events were not associated with history of depression, whereas severe possibly dependent events were significantly associated with first onsets, but not recurrences (Monroe et al., 2007). This suggests that the role of SLEs in the stress-depression association may depend on the independence of events. Further, initial research on the role of LLEs suggests differential associations based on independence. That is, Monroe and colleagues (2006) showed that for patients receiving medication, only independent LLEs focused on the participant predicted recurrence when a 6-week period was considered; for patients not receiving medications, these events predicted fewer recurrences. However, Lenze and colleagues (2008) evidenced the cumulative impact of dependent, not independent, LLEs in predicting recurrences. Further, research on history of childhood adversity has also produced contrasting findings



with sensitization limited to independent LLEs for first onsets specifically in one study (Harkness et al., 2006) and interpersonal (not non-interpersonal) LLEs in another (Rudolph & Flynn, 2008). These findings highlight the need to examine different categories of LLEs, including independence, and to examine the role of LLEs in different populations, including both patient samples (Monroe et al., 2006) and community samples (in the present study).

I examined the impact and occurrence of life events using both cross-sectional and longitudinal within-person analyses. There is agreement in the literature that within-person longitudinal designs that allow examination of the stress-depression relationship across first onsets and recurrences within the same individuals are the most informative and methodologically sound way to test Post's model (e.g., Hammen, 2005). Although contributing to the field extensively (Kendler et al., 2000; Kendler et al., 2001), the few existing within-person longitudinal studies cannot inform of us of the changing role of stress and it does not distinguish between the SS and SA models. The present study expanded on this existing longitudinal research by employing a within-person design to investigate first onsets and first recurrences for events of varying severities with regards to both occurrence and impact, with the aim of elucidating the role of stress and the mechanisms underlying this relationship.

In summary, the analyses in the present study provide the first direct comparison of the models (SS and SA) proposed to underlie the stress-depression association, deemed to be essential for advancing our understanding and refinement of the association (e.g., Monroe & Harkness, 2005). The models' predictions with respect to the impact and occurrence of life events are outlined in Table 2 (see also Monroe & Harkness, 2005).

The SS model predicts that the impact of both SLEs and LLEs will increase, the occurrence of SLEs will decrease, and the occurrence of LLEs will increase with successive recurrences. In contrast, the SA model predicts that the impact and occurrence of both SLEs and LLEs will decrease with successive recurrences. These predictions are not specific to the independence of events, as existing literature on the models does not provide predictions according to this dimension. Testing the models with the strong methods employed in the present study has the potential to refine our understanding of the stress-depression association.

In addition to comparing the underlying models of the stress-depression association, I examined the influence of anxiety on the impact and occurrence of life events in first onsets versus recurrences. Specifically, I examined the influence of the presence of at least one AD before the target event in the impact analyses and the target MDE in the occurrence analyses. Both cross-sectional and longitudinal within-person analyses were employed. As discussed, I predicted that anxiety may sensitize (SS) or kindle (SA) individuals to stress before the first onset of depression (termed presensitized or prekindled subsequently). In other words, I predicted that in individuals with a history of AD, the impact and occurrence of SLEs and LLEs will be similar for first onsets and recurrences. I also examined the influence of the presence of at least one anxiety disorder at the same time as the target event in the impact analyses and the target MDE in the occurrence analyses. I did this to eliminate the possibility that any differences in the impact and occurrence of life events in those with a history of AD as compared to those without a history of AD were due to the presence of a co-existing AD, and not a pre-existing AD. This was an important distinction to fully test the prediction that anxiety

would presensitize or prekindle, rather than only sensitize or kindle. Therefore, we repeated all the analyses for: (1) the presence of a lifetime history of AD; and (2) the presence of concurrent AD.

To summarize, I investigated the associations between stress, depression and anxiety with the aims of: (1) identifying the underlying models of the stress-depression association (SS versus SA); and (2) understanding the influence of comorbid ADs on the stress-depression association.

## METHOD

### Participants

Participants were recruited in two cohorts (summers 1991 and 1992) from the senior classes at three public high schools in Los Angeles County selected to be representative of the county in terms of ethnicity, graduation rate, and post-graduate activities. After consenting to participate (or if under 18, parent consented), all female 12<sup>th</sup> grade students present received an initial questionnaire packet from staff members in their homeroom classes, with most completing it at home and mailing it to the project. Of the nine-hundred-two packets distributed, 513 (57%) were returned and completed, of which 341 provided consent and agreed to be contacted. Three months following graduation, 155 were successfully contacted and scheduled. The reduced number scheduled was due to difficulties contacting participants (due to traveling or moves), transportation difficulties, missed appointments, scheduling difficulties (due to work) and declines based on the time commitment for participation. To evaluate the representativeness of the reduced sample, Hammen and colleagues (e.g, Hammen et al., 2000) conducted two sets of comparisons: (1) comparing the 341 volunteers who agreed to be contacted to the 172 nonvolunteers (who completed the initial questionnaires but did not agree to be contacted); and (2) among the 341 volunteers, comparing the 155 scheduled participants to the 186 who declined or could not be scheduled. Analyses revealed no significant differences for both sets of comparisons for SES (Hollingshead, 1975), ethnicity, self-reported depressive symptoms, and number of behavior problems based on data from the initial questionnaires. Additionally, there were no significant differences between the two cohorts collected (94 first cohort, 61 second cohort), allowing the cohorts to be

combined. As such, in spite of self-selection, the sample was representative of female high school seniors in Los Angeles County.

The 155 female participants began the study with a mean age of 18.29 years (SD = 0.48, range 16-19) and were mostly from middle-class families (mean Hollingshead score = 46.03, SD = 13.18; Hollingshead, 1975). Self-reported ethnicity of the sample was African American, 2%; Asian American, 9%; Caucasian, 46%; Chicana or Latina, 21%; and other (mostly mixed race and Armenian descent), 22%. Of the 155 participants who completed the initial interview, 140 (90%) completed the six-month follow-up; 137 (88%) completed the 1-year follow-up; 134 (87%) completed the 2-year follow-up; 133 (86%) completed the 3-year follow-up; 129 (83%) completed the 4-year follow-up; and 118 (76%) completed the 5-year follow-up. Participants were excluded from the analyses if they developed bipolar I or II symptoms or disorder.

## Procedures and Measures

### *Overview*

All interviews were conducted by licensed clinical psychologists or clinical psychology graduate students. The initial interviews took place during the summer following high school graduation. Participants completed face-to-face interviews, with sessions lasting 2 to 3 hours. Subsequent interviews took place 6 months after the initial interview and then annually for five years, and were conducted over the phone.

### *Axis I Disorders*

Axis I disorders were assessed using the Structured Clinical Interview for the DSM-III-R for non-patient samples (SCID-NP; subsequently referred to as the SCID; Spitzer et al., 1990). Interrater reliability of SCID diagnoses (assessed by independent ratings from

audiotapes) was computed as weighted kappas; .89 (n = 46) for initial interview and .93 (n = 20) for follow-up interviews. The initial interview covered lifetime history of disorders and current symptoms (in the 1-month preceding the initial interview) and subsequent interviews probed the time period (either 6 months for the first follow-up or 1 year for subsequent follow-ups) between interviews. For both past and current symptomatology, depression and anxiety was rated on a 4-point scale with 0 = no symptoms; 1 = mild symptoms; 2 = subthreshold disorder; and 3 = diagnosable disorder.

For the present study, history of depression is defined as meeting full criteria for Major Depression (MDD) prior to the 1-month time period before the initial interview. Forty-five (29%) participants entered the study with a history of MDD and 110 (61%) entered the study without. A new episode of depression was defined as meeting criteria for diagnosable depression. Thirty-four (22%) participants experienced a first onset over the course of the 5-year follow-up period and 34 (22%) experienced a recurrence during the 5-year follow-up period. The range of episodes experienced during the study was 1 to 5: 47 had one episode; 22 had two episodes; 11 had three episodes; 4 had four episodes and 1 had five episodes. The beginning of a new episode was defined as when participants met criteria for diagnosable depression (coded 3 on our rating scale).

History of ADs is defined as meeting full criteria for any AD (except simple phobia) prior to the 1-month time period before the initial interview. Nine participants (6%) entered the study with a history of ADs and 12 (8%) entered the study with a current diagnosable AD. A new episode of anxiety was defined as meeting full criteria for any diagnosable AD (coded 3 on our rating scale) and the beginning of a new episode will be defined as meeting full criteria for a diagnosable disorder. Twenty-two participants

(14.2%) developed at least one diagnosable AD during the study. For all analyses, ADs were collapsed across diagnostic categories, except simple phobia which was excluded due to its high frequency and low associated impairment levels as compared with the other anxiety disorders. Anxiety disorders included were: GAD (11 participants); Social Phobia (6 participants); OCD (4 participants); Panic Disorder (3 participants); and PTSD (3 participants). Eighteen participants had one AD; 1 participant has 2 ADs and 3 participants had 2 ADs.

Two categories of ADs were created: (1) lifetime ADs; and (2) concurrent ADs. Lifetime ADs was defined as the presence of at least one diagnosable AD before the target event in the impact analyses or the target MDE in the occurrence analyses. Concurrent ADs was defined as the presence of at least one diagnosable anxiety disorder at the same time as the target event in the impact analyses or the target MDE in the occurrence analyses. These categories are not mutually exclusive; for example, if participants have ADs prior to the target MDE and at the same time as the target MDE, both lifetime AD and concurrent AD would be coded as present.

### *Stressful Life Events*

Stressful life events were assessed at the initial interview and at each follow-up using an episodic life stress interview that was adapted from Brown's contextual threat assessment method (Brown & Harris, 1978). Participants were probed systematically about the occurrence of life events over the follow-up period using an adapted version of the life events list developed by Paykel and Mangen (1980). Participants were asked to provide information about the context in which the event occurred (e.g., social and financial resources) in order to obtain the degree of impact of the event for a typical

individual given the context surrounding the event. Each event was identified and dated. Interviewers prepared narrative accounts of each event including information such as duration, consequences, and predictability of the event while excluding participants' subjective reactions to events. The narrative accounts were presented to an independent rating team, who were blind to participants' diagnostic information, and who were permitted to query the interviewers about the context surrounding the events. Subsequently, the rating team (composed of staff members) rated the objective impact of the events on a scale from 1 (no negative impact) to 5 (extremely severe negative impact). In addition, the rating team rated the independence of the events on a scale from 1 (fully independent of the person's behavior; e.g., death of relative) to 5 (fully dependent; occurred strictly as a result of the person's own actions; e.g., failed important exam because she did not study for it). Events coded as 3 or higher were considered to be at least partly the result of the participant's own actions and were coded as dependent for the analyses. A second masked team re-rated a set of events on objective impact and independence versus dependence; the intraclass correlation coefficients for the ratings made by the independent teams were .92 ( $n = 74$ ) for objective stress and .97 ( $n = 53$ ) for independence versus dependence.

For the present study, SLEs were defined as events rated 3.0 and higher and LLEs were defined as 2.5 and lower. A large percentage of participants experienced LLEs during the 5-year study period (96% for independent LLEs and 100% for dependent LLEs) and a moderate percentage of participants experienced SLEs (72% for independent SLEs and 70% for dependent SLEs). Life event calendars were created for each participant listing all life events along with their objective impact score, independence



score, and date of occurrence. Each event on the life event calendar was numbered according to the order in which it occurred during the study period. In addition, timelines charting Major Depressive Episodes (MDEs) and life events, dating each event and each episode beginning, were created to assure that events preceded episodes.<sup>1</sup> Life events occurring 3 months prior to the onset of new episodes were included in the analyses. This interval provides temporal sensitivity and it is consistent with other research examining the role of life events and depression (e.g., Daley, Hammen & Rao, 2000).

### *Data Analyses*

#### *Cross Sectional Analyses Examining the SS versus SA Models*

Identical analyses were conducted for both types of SLEs and LLEs. The impact of events was defined as the conditional probability of an episode of depression given the presence of an SLE or LLE ( $P[\text{MDE}|\text{SLE}]$  or  $P[\text{MDE}|\text{LLE}]$ ) and the occurrence of events was defined as the conditional probability of an SLE or LLE given the presence of an MDE ( $P[\text{SLE}|\text{MDE}]$  or  $P[\text{LLE}|\text{MDE}]$ ; Monroe & Harkness, 2005). To calculate the conditional probabilities, Bayes' Theorem was followed such that the conditional probability of B given A ( $P[B|A]$ ) is the probability of A and B divided by the probability of A ( $P[A \text{ and } B] / P[A]$ ). For all analyses, one conditional probability was calculated for participants with a history of depression (DHX+) and one for participants with no history of depression (DHX-). The conditional probabilities were compared using a two-tailed z-test with pooled standard error and a 95% confidence interval using a z-test for two proportions calculator found online (Dimension Research, n.d.). If the proportions were exactly equal the test was not performed.

*Impact.* For both the SLE and LLE analyses, the conditional probabilities of an MDE given the presence of an SLE [ $P(\text{MDE}|\text{SLE})$ ] or LLE [ $P(\text{MDE}|\text{LLE})$ ] were compared for first onsets versus recurrences. In order to compute the probabilities for SLEs, the timelines were used to select the most severe independent and dependent SLEs occurring in the study for each participant. If a participant experienced more than one event at the highest level of severity, then the first of those events was selected. A second set of probabilities were computed for SLEs; in these analyses a random SLE was selected for each participant, rather than the most severe SLE. We examined both a random SLE and the most severe SLE because it is possible that the most severe SLEs continue to be potent with successive recurrences, but that SLEs in general may decrease in impact (Monroe & Harkness, 2005) In order to compute the probabilities for LLEs, the timelines were used to select a random independent and dependent LLE to capture a range of events occurring at various points of the study. In order to identify randomly selected SLEs and LLEs, the life event calendars were used to select events. All events on the life event calendars were numbered. For each participant, the total number of events was recorded. Then, a number was randomly chosen from 1 to the total number of events until one event from each category (independent and dependent SLEs and LLEs) was selected. Because the life event calendars did not include information about Axis I disorders, we could ensure event selection was not biased by the presence of disorders. The event and date were then recorded and then the timelines were used to examine the three months following the events for the presence or absence of an MDE; to be included the beginning of the MDE (onset date) had to be within 3 months following the event date. Thus, the presence or absence of an MDE was recorded for all 6 types of events (independent SLE

[most severe and randomly selected], dependent SLE [most severe and randomly selected]), independent LLE, and dependent LLE). As noted in the hypotheses and in Table 2, for SLEs, both models will be supported if  $P(\text{MDE}|\text{SLE})$  for recurrences is less than  $P(\text{MDE}|\text{SLE})$  for first onsets. For LLEs, the SS model will be supported if  $P(\text{MDE}|\text{LLE})$  for recurrences is greater than  $P(\text{MDE}|\text{LLE})$  for first onsets whereas the SA model will be supported if  $P(\text{MDE}|\text{SLE})$  recurrences is less than  $P(\text{MDE}|\text{LLE})$  for first onsets.

*Occurrence.* For both the SLE and LLE analyses, the conditional probabilities of an SLE or LLE given the presence of an MDE [ $P(\text{SLE}|\text{MDE})$  or  $P(\text{LLE}|\text{MDE})$ ] were compared for first onsets versus recurrences. To compute the probabilities, the timelines were used to select the first MDE occurring in the study for each participant. The three months preceding the onset of the episode were examined for the presence or absence of independent and dependent SLEs and LLEs. Thus, a presence or absence score was given for all four types of events in the 3 month period for the episode selected. Thus, 4 sets of conditional probabilities were compared, the conditional probability for first onsets versus recurrences for 4 types of events (independent SLE, dependent SLE, independent LLE, and dependent LLE). As noted in the hypotheses and in Table 2, the SS model will be supported if  $P(\text{SLE}|\text{MDE})$  for recurrences is greater than  $P(\text{SLE}|\text{MDE})$  for first onsets whereas the SA model will be supported if  $P(\text{SLE}|\text{MDE})$  for recurrences is less than  $P(\text{SLE}|\text{MDE})$  for first onsets. For LLEs, the SS model will be supported if  $P(\text{LLE}|\text{MDE})$  for recurrences is greater than  $P(\text{LLE}|\text{MDE})$  for first onsets whereas the SA model will be supported if  $P(\text{LLE}|\text{MDE})$  for recurrences is less than  $P(\text{LLE}|\text{MDE})$  for first onsets.

*Longitudinal Within-Person Analyses Examining the SS versus SA Models*

Analyses were conducted using a multi-level logistic regression approach with repeated measures nested (over the 6 time points) within-persons and heterogeneous compound variance structure. All variables were dichotomous (e.g., presence of MDE at time 1: 1=yes, 0=no; history of MDE (for corresponding time point): 1=yes, 0=no; presence of event in 3 mo prior to MDE (for corresponding time point): 1=yes, 0=no). For both impact and occurrence, the analyses were repeated for the four types of events (independent SLE, independent LLE, dependent SLE, and dependent LLE). All interactions were tested in multi-level logistic regression analyses after entering the main effects (Cohen, Cohen, West, & Aiken, 2003).

*Impact.* The outcome variable was the presence of MDE. The fixed effects were presence of life event, history of MDE and their two-way interaction. For each type of event, one event of was selected during each of the 6 time points and the 3 months following the event were examined for the presence of MDE. If an event of each type did not occur during the time point, then a random period was selected and examined for the presence of MDEs. The interaction of history of MDE and the presence of life events reflects whether the association of the impact of life events and depression is different for first onsets and recurrences. Therefore, for SLEs: (1) the SS model will be supported if SLEs have a stronger association with MDE among people with recurrences than among people with first onsets; or (2) the SA model will be supported if SLEs have a stronger association with MDE among people with first onsets than among people with recurrences. For LLEs because the predictions are the same, the same would hold true.

*Occurrence.* The outcome variable was the presence of the event (independent SLE, independent LLE, dependent SLE or dependent LLE). The fixed effects were presence of

MDE, history of MDE and their two-way interaction. All MDEs occurring during the study period were selected and the 3 months prior to the episode were examined for the presence of each of the 4 types of events. If an MDE did not occur during the study period, then a random 3 month period was selected and examined for the presence of each of the 4 types of events. The interaction between history of MDE and presence of MDE reflected whether the association of the occurrence of life events and depression is different for first onsets and recurrences. For SLEs, the SS and SA models will be supported if MDEs have a stronger association with SLEs among people with first onsets than among people with recurrences. For LLEs, (1) the SS model will be supported if MDEs have a stronger association with LLEs among people with recurrences than among people with first onsets; or (2) the SA model will be supported if MDEs have a stronger association with LLEs among people with first onsets than among people with recurrences.

#### *Cross-Sectional Analyses Examining the Influence of Comorbid Anxiety*

Twenty separate hierarchical logistic regressions were conducted with history of MDE as the dependent variable: twelve analyses examined impact and eight analyses examined occurrence. For both impact and occurrence, separate analyses were conducted for each of the four types of life events: dependent SLE, dependent LLE, independent SLE and independent LLE. We also examined both the worst (most severe during the study period) and randomly-selected SLEs for impact. In addition, analyses were conducted for the two anxiety disorder categories: the presence of lifetime ADs and the presence of concurrent ADs. All interactions were tested in hierarchical logistic regression analyses after entering the main effects (Cohen et al., 2003).

The data analytic procedure was based on the only published report to examine occurrence by Monroe and colleagues. Monroe et al., (2007) used hierarchical regression to predict variation in depression history (episode number), from the presence or absence of severe difficulties and the presence or absence of SLEs and their interaction among a sample of participants who had an MDE. Following this strategy, to examine occurrence, we included only participants who had an MDE and entered the presence of events as a main effect (along with the relevant anxiety variable, as is described further below). As in the conditional probability analyses, events had to occur within 3 months of the beginning of the target MDE to be coded as present. Because all participants included in the analysis had an MDE, this is analogous to the definition for occurrence: the presence of an event given an MDE. Thus, this replicates the cross-sectional occurrence analyses using logistic regression rather than conditional probabilities.

To examine impact, we reversed this procedure. To be included in the analyses, participants had to experience the target event and we entered the presence of MDE in the 3 months following the target event as a main effect (again along with the relevant anxiety variable) to predict depression history. Because all participants included in the analysis had an event, this is analogous to the definition for impact: the presence of an MDE given an event. Thus, this replicates the cross-sectional impact analyses using logistic regression rather than conditional probabilities.

Unlike Monroe et al. (2007), we did not have information on episode number for our outcome variable. Therefore, we used a dichotomous outcome variable for history of depression, rather than a continuous one (as in Monroe et al., 2007). As a result, we used logistic regression, rather than hierarchical linear regression.

*Impact.* As discussed, to examine the likelihood of a first onset versus a recurrence given the presence of a life event, participants had to experience the target event in order to be included in the analysis. In each analysis, the presence or absence of MDE in the 3 months following the target event was entered first, the presence or absence of anxiety disorders was entered the second, followed by their interaction. The outcome variable was depression history.

In accordance with Post's model, I predicted that the presence of MDE (following the target event) will be significantly associated with history of depression, indicating that the impact of the target event differs as a function of depression history. This replicates the cross-sectional impact analyses.

I also predicted that the interaction between the event and the presence of anxiety will be significant, reflecting that the impact of life events depends on the presence of lifetime AD. Specifically, for those without lifetime AD, the presence of MDEs will be significantly associated with history of depression. This will suggest that the impact of events is different for those with and without a history of depression, supporting Post's model. However, for those with a lifetime AD, the presence of MDEs will not be significantly associated with history of depression. This reflects that the impact of events is similar for those with and without a history of depression, supporting the hypothesis that the presence of lifetime AD presensitizes or prekindles individuals to stress, before the first episode of depression.

*Occurrence.* To examine the likelihood of a first onset versus a recurrence given the presence of an MDE, participants had to experience an MDE during the study to be included in the analysis. In each analysis, the presence or absence of an event in the 3

months prior to the target MDE was entered first, the presence or absence of AD was entered second, followed by the interaction. The outcome variable was depression history.

In accordance with Post's model, I predicted that the presence of the target event (in the 3 months prior to an MDE) will be significantly associated with history of depression, indicating that the occurrence of events is different for first onsets and recurrences. This replicates the cross-sectional occurrence analyses.

I also predicted that the interaction between the presence of the target event and the presence of lifetime AD will be significant, reflecting that the occurrence of life events depends on the presence of lifetime AD. Specifically, for those without lifetime AD, the presence of the target event will be significantly associated with history of depression, suggesting that the occurrence of events is different for first onsets and recurrences. This will support Post's model. However, for those with a lifetime AD, the presence of the target event will not be associated with history of depression, suggesting that the occurrence of events is similar for first onsets and recurrences. This will support the hypothesis that the presence of lifetime AD presensitizes or prekindles individuals to stress, before the first episode of depression.

#### *Longitudinal Within-Person Analyses Examining the Influence of Comorbid Anxiety*

Analyses were conducted using a multi-level logistic regression approach with repeated measures nested (over the 6 time points) within-persons and heterogeneous compound variance structure. All variables were dichotomous and defined as yes (coded 1) or no (coded 0). Analyses were repeated for the four types of life events (independent SLE, independent LLE, dependent SLE and dependent LLE) for both lifetime AD and concurrent (8 total analyses for each impact and occurrence). All interactions were tested



in multi-level logistic regression analyses after entering the main effects (Cohen et al., 2003).

*Impact.* The outcome variable was the presence of MDE. The fixed effects were the presence of life event, history of depression, presence of AD, their two-way interactions, and the three-way interaction. If each of the 4 types of events did not occur, during each of the 6 time points, then a random three month period was selected during each time point and examined for the presence of MDEs and ADs. The three-way interaction reflected whether there was a different association between the impact of life events and MDE for first onsets and recurrences based on the presence of anxiety.

As in the first set of longitudinal within-person analyses discussed previously, the interaction of history of MDE and the presence of life events reflects whether the impact of life events on depression is different for first onsets and recurrences. This replicates the longitudinal within-person analyses examining impact.

I predicted that the 3-way interaction between the presence of the target event, history of depression, and the presence of lifetime AD will be significant. Specifically, for those without lifetime AD, I predicted that the two-way interaction between the presence of events and history of depression would be significant. For both SLEs and LLEs, if the interaction reveals that the association is stronger among those with a history of depression, it will reflect support for the SS model. However, if the interaction reveals that the association is stronger among those without a history of depression, it will reflect support for the SA model. In contrast, for those with lifetime AD, I predicted that the two-way interaction between the presence of events and history of depression will not be significant, reflecting that the occurrence of events does not depend on history of

depression. This will support the prediction that lifetime AD presensitizes or prekindles individuals to stress, before the first episode of depression.

*Occurrence.* The outcome variable was the presence of an event. The fixed effects were the presence of MDE, history of depression, presence of AD, their two-way interactions, and the three-way interaction. If a participant did not experience an MDE in the study, a 3 month random period was selected and examined for the presence of each of the four types of events and the two types of AD. The three-way interaction reflected whether there was a different association between the occurrence of life events and depression based on the presence of anxiety.

The interaction between history of MDE and presence of MDEs reflected whether the association of the occurrence of life events and depression is different for first onsets and recurrences. This replicates the longitudinal within-person analyses examining occurrence.

I predicted that the 3-way interaction between the presence of MDEs, history of depression, and the presence of lifetime AD will be significant. Specifically, for those without lifetime AD, I predicted that the two-way interaction between the presence of MDEs and history of depression would be significant. For SLEs, the SS and SA models will be supported if MDEs have a stronger association with SLEs among people with first onsets than among people with recurrences. For LLEs, (1) the SS model will be supported if MDEs have a stronger association with LLEs among people with recurrences than among people with first onsets; or (2) the SA model will be supported if MDEs have a stronger association with LLEs among people with first onsets than among people with recurrences. In contrast, I predicted that the two-way interaction between the presence of

MDEs and history of depression will not be significant for those with lifetime AD, reflecting that the occurrence of events does not depend on history of depression. This will support the prediction that lifetime AD presensitizes or prekindles individuals to stress, before the first episode of depression.

## RESULTS

### Cross-Sectional Analyses Examining the SS versus SA Models

#### *Impact*

A summary of the calculations for computing the impact of life events is shown in Table 3.

#### *Independent SLEs*

*Worst independent SLE.* The conditional probability ( $P[MDE|SLE]$ ) for the most severe independent SLEs was .30 for individuals with a history of depression whereas the conditional probability ( $P[MDE|SLE]$ ) was .11 for individuals without a history of depression. The proportions were significantly different ( $z = 2.70; p < .05$ ), with a two-tailed confidence level of 99.3%. This indicates that the impact of the most severe independent SLEs increased with repeated episodes, such that the probability of experiencing an MDE following the presence of an independent SLE is greater for recurrences than first onsets. This supports the SS model.

*Randomly-selected independent SLE.* The conditional probability ( $P[MDE|SLE]$ ) for the randomly-selected independent SLEs was .33 for individuals with a history of depression whereas the conditional probability ( $P[MDE|SLE]$ ) was .07 for individuals without a history of depression. The proportions were significantly different ( $z = 3.89; p < .05$ ), with a two-tailed confidence level of 100%. Mirroring the prior analysis, this indicates that the impact of the most severe independent SLEs increased with repeated episodes, such that the probability of experiencing an MDE following the presence of an independent SLE, is greater for recurrences than first onsets. This supports the SS model.

#### *Independent LLEs*

The conditional probability ( $P[\text{MDE}|\text{LLE}]$ ) for independent LLEs was .17 for individuals with a history of depression and the conditional probability ( $P[\text{MDE}|\text{LLE}]$ ) was .03 for individuals without a history of depression. The proportions were significantly different ( $z = 2.62; p < .05$ ), with a two-tailed confidence level of 99.1%. This indicates that the impact of independent SLEs increased with repeated episodes, such that the probability of experiencing an MDE following the presence of an independent SLE, is greater for recurrences than first onsets. This supports the SS model.

#### *Dependent SLEs*

*Worst dependent SLE.* The conditional probability ( $P[\text{MDE}|\text{SLE}]$ ) for the most severe dependent SLEs was .10 for individuals with a history of depression and the conditional probability ( $P[\text{MDE}|\text{SLE}]$ ) was .09 for those without a history of depression ( $z = -.08; p > .05$ ). This indicates that the impact of the most severe dependent SLEs remained constant with repeated episodes, such that the probability of experiencing an MDE following the presence of a dependent SLE is the same for first onsets and recurrences. This does not support the SA or SS models.

*Randomly-selected dependent SLE.* The conditional probability ( $P[\text{MDE}|\text{SLE}]$ ) for a randomly-selected dependent SLEs was .16 for individuals with a history of depression and the conditional probability ( $P[\text{MDE}|\text{SLE}]$ ) was .09 for those without a history of depression ( $z = 1.05; p > .05$ ). As with the prior analysis, this indicates that the impact of randomly-selected dependent SLEs remained constant with repeated episodes, such that the probability of experiencing an MDE following the presence of a dependent SLE is the same for first onsets and recurrences. This does not support the SS or SA models.

### *Dependent LLEs*

The conditional probability ( $P[MDE|LLE]$ ) for dependent LLEs was .08 for individuals with a history of depression and the conditional probability ( $P[MDE|LLE]$ ) was .05 for individuals without a history of depression ( $z = .41; p > .05$ ). This indicates that the impact of dependent lower life events remains the same with repeated episodes, such that the probability of MDE, given the presence of an LLE, is the same for recurrences and first onsets. This does not support the SS or SA models.

### *Occurrence*

A summary of the calculations for computing the impact of life events is shown in Table 4.

### *Independent SLEs*

The conditional probability ( $P[SLE|MDE]$ ) for independent SLEs was .29 for individuals with a history of depression and the conditional probability ( $P[SLE|MDE]$ ) was .27 for individuals without a history of depression ( $z = .06, p > .05$ ). This indicates that the occurrence of independent SLEs remains constant with repeated episodes, such that the probability of a precipitating SLE, given an MDE, is the same for recurrences and first onsets. This does not support the SS or SA models.

### *Independent LLEs*

The conditional probability ( $P[LLE|MDE]$ ) for independent LLEs was .29 for individuals with a history of depression whereas the conditional probability ( $P[LLE|MDE]$ ) was .27 for individuals without a history of depression ( $z = .06, p < .05$ ). This indicates that the occurrence of independent LLEs remains the same with repeated

episodes, such that the probability of a precipitating LLE, given an MDE, is the same for recurrences and first onsets. This does not support the SS and SA models.

#### *Dependent SLEs*

The conditional probability ( $P[SLE|MDE]$ ) for dependent SLEs was .14 for individuals with a history of depression whereas the conditional probability ( $P[SLE|MDE]$ ) was .35 for those without a history of depression ( $z = 2.44, p < .05$ ), with a two-tailed confidence interval of 98.5%. This indicates that the occurrence of dependent SLEs decreased with repeated episodes, such that the probability of a precipitating SLE, given an MDE, is greater for first onsets than recurrences. This supports the SS and SA models.

#### *Dependent LLEs*

The conditional probability ( $P[LLE|MDE]$ ) for dependent LLEs was .53 for individuals with a history of depression whereas the conditional probability ( $P[LLE|MDE]$ ) was .70 for individuals without a history of depression ( $z = 1.84, p > .05$ ). This indicates that the occurrence of dependent LLEs remains the same with repeated episodes, such that the probability of a precipitating LLE, given an MDE, is the same for recurrences and first onsets. This does not support the SS and SA models.

#### Longitudinal Within-Person Analyses Examining the SS versus SA Models

The frequencies of life events in the within-person longitudinal analyses for the impact and occurrence of life events are presented in Table 5.

#### *Impact*

The estimates,  $t$  values and  $p$  values are presented in Table 6.

#### *Independent Events*

*Independent SLEs.* At each time point, there was not a significant association between the presence of an independent SLE and the presence of MDEs ( $p > .05$ ). At each time point, there was a significant positive association of the presence of history of MDE and the presence of MDEs ( $p < .05$ ), indicating that history of MDE is associated with greater likelihood of MDEs. In addition, the interaction of the presence of independent SLEs and the history of depression was not significant ( $p > .05$ ). This does not support Post's model.

*Independent LLEs.* At each time point, there was not a significant association between the presence of an independent LLE and the presence of MDEs ( $p > .05$ ). At each time point, there was a significant positive association of the presence of history of MDE and the presence of MDEs ( $p < .05$ ), indicating that history of MDE is associated with greater likelihood of MDEs. In addition, the interaction of the presence of independent LLEs and the history of depression was not significant ( $p > .05$ ). This does not support Post's model.

#### *Dependent Events*

*Dependent SLEs.* At each time point, there was not a significant association between the presence of a dependent SLE and the presence of MDEs ( $p > .05$ ). At each time point, there was a significant positive association of the presence of history of MDE and the presence of MDEs ( $p < .05$ ), indicating that history of MDE is associated with greater likelihood of MDEs. In addition, the interaction of the presence of dependent SLEs and the history of depression was not significant ( $p > .05$ ). This does not support Post's model.



*Dependent LLEs.* At each time point, there was a significant negative association between the presence of a dependent LLE and the presence of MDEs ( $p < .05$ ), indicating that the presence of dependent LLEs is associated with lower likelihood of MDEs. At each time point, there was a significant positive association of the presence of history of MDE and the presence of MDEs ( $p < .05$ ), indicating that history of MDE is associated with greater likelihood of MDEs. In addition, the interaction of the presence of dependent LLEs and history of depression is significant ( $p < .05$ ). Specifically, for those with a history of depression, at each time point, there was a significant negative association between the presence of a dependent LLEs and the presence of MDEs ( $estimate = -.214$ ;  $t = -6.26$ ;  $p = .00$ ). In contrast, for those without a history of depression, at each time point, there was not a significant association between the presence of a dependent LLE and the presence of MDEs ( $estimate = -.038$ ;  $t = .49$ ;  $p = .62$ ). This suggests that the association between the presence of events and the presence of MDEs is stronger among those with a history of depression. Because the association is more strongly negative, this suggests that events are less likely to be followed by MDEs among those with a history of depression. That is, the occurrence of dependent LLEs is lower among those with a history of depression. This supports the SA model.

#### *Occurrence*

The estimates,  $t$  values and  $p$  values are presented in Table 7.

#### *Independent Events*

*Independent SLEs.* At each time point, the presence of MDEs was positively associated with the presence of independent SLEs ( $p < .05$ ). At each time point, history of depression was not significantly associated with the presence of independent SLEs ( $p$

> .05). The interaction of the presence of MDEs and history of depression was not significant ( $p > .05$ ), indicating that the occurrence of independent SLEs does not depend on history of depression. This does not support Post's model.

*Independent LLEs.* At each time point, the presence of MDEs was not associated with the presence of independent LLEs ( $p < .05$ ). At each time point, history of depression was not significantly associated with the presence of independent LLEs ( $p > .05$ ). The interaction of the presence of MDEs and history of depression was not significant ( $p > .05$ ), indicating that the occurrence of independent LLEs does not depend on history of depression. This does not support Post's model.

#### *Dependent Events*

*Dependent SLEs.* At each time point, the presence of MDEs was positively associated with the presence of dependent SLEs ( $p < .05$ ). At each time point, history of depression was not significantly associated with the presence of dependent SLEs ( $p > .05$ ). The interaction of the presence of MDEs and history of depression was significant ( $p < .05$ ), indicating that the occurrence of dependent SLEs depends on history of depression. Specifically, for first onsets, the presence of MDEs was positively associated with the presence of dependent SLEs ( $estimate = .469$ ;  $t = 4.12$ ;  $p = .00$ ). For recurrences, the presence of MDEs was also positively associated with the presence of dependent SLEs ( $estimate = .145$ ;  $t = 2.40$ ;  $p = .02$ ). This suggests that the association is stronger for first onsets than recurrences. In other words, the occurrence of dependent SLEs is greater for first onsets than recurrences. This supports both the SS and SA models.

*Dependent LLEs.* At each time point, the presence of MDEs was not associated with the presence of dependent LLEs ( $p < .05$ ). At each time point, history of depression was

not significantly associated with the presence of dependent LLEs ( $p > .05$ ). The interaction of the presence of MDEs and history of depression was not significant ( $p > .05$ ), indicating that the occurrence of dependent LLEs does not depend on history of depression. This does not support Post's model.

#### Cross-Sectional Analyses Examining the Influence of Comorbid Anxiety

The frequencies of lifetime AD and concurrent AD for the impact and occurrence analyses are presented in Table 8.

#### *Impact*

The coefficients, Wald Chi-Square Statistics, standard errors and p values are presented in Table 9 for lifetime AD and Table 10 for concurrent AD.

#### *Independent Events*

*Lifetime AD.* In the analyses for worst and randomly selected independent SLEs and independent LLEs, the presence of MDE (in the 3 months following independent events) was significantly associated with history of depression ( $ps < .05$ ). Replicating the cross-sectional conditional probability analyses, this indicates that MDEs are more likely to be present following independent events in individuals with a history of depression. In addition, the presence of lifetime AD (the presence of at least one AD before the event) was significantly associated with history of depression ( $p < .05$ ). This indicates lifetime ADs are more likely to be present in individuals with a history of depression. The interaction of lifetime ADs and the presence of MDEs was not significant ( $p > .05$ ). Taken together, these analyses suggest that the impact of independent SLEs and LLEs is greater in individuals with a history of depression as compared to those without a history

of depression, supporting the SS model. However, the impact of independent SLEs and LLEs does not depend on the presence of lifetime AD (see Table 9).

*Concurrent AD.* In the analyses for the worst and randomly selected independent SLEs and independent LLEs, the presence of MDE (in the 3 months following independent events) was significantly associated with history of depression ( $ps < .05$ ). Replicating the cross-sectional conditional probability analyses, this indicates that MDEs are more likely to be present following independent events in individuals with a history of depression. The presence of concurrent AD (at the time of the event) was not significantly associated with history of depression ( $p > .05$ ). The interaction of concurrent ADs and the presence of MDEs was not significant ( $p > .05$ ) for randomly selected SLEs and LLEs. However, for the worst independent SLE, the interaction could not be tested, as only 1 participant had concurrent AD in this analysis. Taken together, similar to above, these analyses suggest that the impact of independent SLEs and LLEs is greater in individuals with a history of depression as compared to those without a history of depression, supporting the SS model. However, the impact of independent randomly selected SLEs and LLEs does not depend on the presence of concurrent AD (see Table 10).

#### *Dependent Events*

*Lifetime AD.* In the analyses for worst and randomly selected dependent SLEs and dependent LLEs, the presence of MDE in the 3 months following dependent events was not associated with history of depression ( $ps > .05$ ). Replicating the cross-sectional conditional probability analyses, this indicates that MDEs are equally likely to be present following dependent events in individuals with and without a history of depression. In

addition, the presence of lifetime AD (the presence of at least one AD before the event) was not associated with a history of depression for worst or randomly selected dependent SLEs ( $ps > .05$ ). However, the presence of lifetime AD was significantly associated with history of depression for dependent LLEs ( $p < .05$ ). This indicates lifetime ADs occurring before dependent LLEs are more likely to be present in individuals with a history of depression. The interaction of lifetime ADs and the presence of MDEs was not significant ( $p > .05$ ). Taken together, these analyses suggest that the impact of dependent SLEs and LLEs does not depend on history of depression. This does not support Post's model. In addition, the impact of dependent events does not depend on the presence of lifetime AD (see Table 9).

*Concurrent AD.* In the analyses for worst and randomly selected dependent SLEs and dependent LLEs, the presence of MDE in the 3 months following dependent events, was not associated with history of depression ( $ps > .05$ ). Replicating the cross-sectional conditional probability analyses, this indicates that MDEs are equally likely to be present following dependent events in individuals with and without a history of depression. In addition, the presence of concurrent AD (the presence of at least one AD at the same time as the event occurred), was not associated with a history of depression ( $p > .05$ ). The interaction of concurrent ADs and the presence of MDEs was not significant for SLEs ( $p > .05$ ). For LLEs the interaction could not be tested, as only 1 participant had concurrent AD in this analysis. Taken together, these analyses suggest that the impact of dependent SLEs and LLEs does not depend on history of depression. This does not support Post's model. In addition, the impact of dependent SLEs does not depend on the presence of concurrent AD; its' influence on dependent LLEs is unknown (see Table 10).

### *Occurrence*

The coefficients, Wald Chi-Square Statistics, standard errors and p values are presented in Table 11 for lifetime AD and Table 12 for concurrent AD.

#### *Independent Events*

*Lifetime AD.* Neither the presence of independent SLEs nor LLEs (in the 3 months prior to an MDE) were associated with history of depression ( $ps > .05$ ). Replicating the cross-sectional conditional probability analyses, this indicates that independent events are equally likely to be present prior to first onsets and recurrences of depression. In addition, the presence of lifetime AD (the presence of at least one AD before the MDE) was not associated with history of depression ( $p > .05$ ). The interaction of lifetime ADs and the presence of independent events was not significant ( $p > .05$ ). Taken together, these analyses suggest that the occurrence of independent SLEs and LLEs does not depend on history of depression. This does not support Post's model. In addition, the occurrence of dependent events does not depend on the presence of lifetime AD (see Table 11).

*Concurrent AD.* Neither the presence of independent SLEs nor LLEs (in the 3 months prior to an MDE) were associated with history of depression ( $ps > .05$ ). Replicating the cross-sectional conditional probability analyses, this indicates that independent events are equally likely to be present prior to first onsets and recurrences of depression. In addition, the presence of concurrent AD (the presence of at least one AD at the same time as the MDE) was not associated with history of depression ( $p > .05$ ). The interaction of concurrent ADs and the presence of independent events was not significant ( $p > .05$ ). Taken together, these analyses suggest that the occurrence of independent SLEs and LLEs does not depend on history of depression. This does not support Post's model. In

addition, the occurrence of independent events does not depend on the presence of concurrent AD (see Table 12).

### *Dependent Events*

*Lifetime AD.* Neither the presence of dependent SLEs nor LLEs (in the 3 months prior to an MDE) were associated with history of depression ( $p > .05$ ). This indicates that dependent events are equally likely to be present prior to first onsets and recurrences of depression. This replicates the finding that the occurrence of dependent LLEs does not vary in first onsets and recurrences from the cross-sectional conditional probability analyses; but, it is inconsistent with the finding from those analyses that reflected changes in the occurrence of dependent SLEs as a function of depression history. In addition, the presence of lifetime AD (the presence of at least one AD before the MDE), was not associated with history of depression for dependent LLEs ( $p > .05$ ), but it was significantly associated with history of depression for dependent SLEs ( $ps < .05$ ). This indicates that the presence of lifetime AD (before an MDE with a prior dependent SLE) is associated with a higher likelihood of depression history. The interaction of lifetime ADs and the presence of dependent events was not significant ( $p > .05$ ). Taken together, these analyses suggest that the occurrence of dependent SLEs and LLEs does not depend on history of depression. This does not support Post's model. In addition, the occurrence of dependent events does not depend on the presence of lifetime AD (see Table 11).

*Concurrent AD.* Neither the presence of dependent SLEs nor LLEs (in the 3 months prior to an MDE) were associated with history of depression ( $ps > .05$ ). As above, this indicates that dependent events are equally likely to be present prior to first onsets and recurrences of depression, only partially replicating the cross-sectional conditional

probability analyses. In addition, the presence of concurrent AD (the presence of at least one AD at the same time as the MDE) was not associated with a history of depression ( $p > .05$ ). The interaction of concurrent ADs and the presence of dependent events was not significant ( $p > .05$ ). Taken together, these analyses suggest that the occurrence of dependent SLEs and LLEs does not depend on history of depression. This does not support Post's model. In addition, the occurrence of dependent events does not depend on the presence of concurrent AD (see Table 12).

#### Longitudinal Within-Person Analyses Examining the Influence of Comorbid Anxiety

##### *Impact*

See Table 13 for a summary of the analyses. The number of lines with AD present was 88-90 (11.2% - 11.5%) for the lifetime AD analyses and 19 (2.4%) for the concurrent AD analyses.

##### *Independent SLEs*

*Lifetime AD.* At each time point, there was not a significant association between the presence of MDEs and the presence of independent SLEs ( $p > .05$ ). At each time point, there also was not a significant association between the presence of MDEs and the presence of lifetime AD ( $p > .05$ ). There was a significant positive association between history of depression and the presence of MDEs at each time point ( $p < .01$ ). The 2-way and 3-way interactions were not significant ( $ps > .05$ ). This indicates that the impact of independent SLEs is similar for first onsets and recurrences. This does not support Post's model. In addition, the impact of independent SLEs does not depend on the presence of lifetime AD.



*Concurrent AD.* Similar to above, at each time point, there was not a significant association between the presence of MDEs and the presence of independent SLEs ( $p > .05$ ). At each time point, there also was not a significant association between the presence of MDEs and the presence of concurrent AD ( $p > .05$ ). There was a significant positive association between history of depression and the presence of MDEs following independent SLEs at each time point ( $p < .01$ ). The 2-way interaction of the presence of independent SLEs and history of MDE was not significant ( $p > .05$ ), indicating that the impact of independent SLEs does not depend on history of depression. The 2-way interaction of the presence of concurrent AD and history of MDE was significant ( $p < .01$ ). Specifically, for individuals without a history of depression, there was not a significant association between the presence of concurrent AD and the presence of MDEs (estimate =  $-.300$ ;  $t = -1.46$ ;  $p = .15$ ). For individuals with a history of depression, there was a significant positive association between the presence of concurrent AD and the presence of an MDE (estimate =  $.219$ ;  $t = 2.68$ ;  $p = .00$ ). This suggests that the presence of concurrent AD is associated with a higher likelihood of MDE for individuals with a history of depression, whereas the presence of concurrent AD is not associated with MDE for those without a history of depression. The 2-way interaction of the presence of concurrent AD and the presence of independent SLEs was significant ( $p < .01$ ). Specifically, for those with concurrent ADs, there was a negative association between the presence of an independent SLE and the presence of an MDE (estimate =  $-.069$ ;  $t = -1.65$ ;  $p = .10$ ). For those without concurrent ADs, there was a significant positive association between the presence of an independent SLE and the presence of an MDE (estimate =  $.135$ ;  $t = 3.25$ ;  $p = .00$ ). This suggests that independent SLEs are less likely to be

followed by MDEs for individuals with concurrent AD, whereas independent SLEs are more likely to be followed by MDEs for those without concurrent AD. The 3-way interaction was not able to be tested because all participants with concurrent AD and a history of depression had an independent SLE. Thus, the influence of concurrent AD on the impact of independent SLEs as a function of depression history is unknown.

#### *Independent LLEs*

*Lifetime AD.* At each time point, there was not a significant association between the presence of MDEs and the presence of independent LLEs ( $p > .05$ ). At each time point, there also was not a significant association between the presence of MDEs and the presence of lifetime AD ( $p > .05$ ). There was a significant positive association between history of depression and the presence of MDEs at each time point ( $p < .01$ ). The 2-way and 3-way interactions were not significant ( $ps > .05$ ). This indicates that the impact of independent LLEs is similar for those with and without a history of depression. This does not support Post's model. In addition, the impact of independent LLEs does not depend on the presence of lifetime AD.

*Concurrent AD.* Similar to above, at each time point, there was not a significant association between the presence of MDEs and the presence of independent LLEs ( $p > .05$ ). At each time point, there also was not a significant association between the presence of MDEs and the presence of concurrent AD ( $p > .05$ ). There was a significant positive association between history of depression and the presence of MDEs at each time point ( $p < .01$ ). The 2-way interaction of the presence of independent LLEs and history of MDE was not significant ( $p > .05$ ). This indicates that the impact of independent LLEs does not depend on history of depression. This does not support Post's

model. The 2-way interaction of the presence of concurrent AD and history of MDE was significant ( $p < .01$ ). Specifically, for those without a history of depression, there was not a significant association between concurrent AD and the presence of MDEs (estimate =  $-.260$ ;  $t = -1.33$ ;  $p = .18$ ). For those with a history of depression, there was a positive significant association between concurrent AD and the presence of MDEs (estimate =  $.180$ ;  $t = 2.42$ ;  $p = .02$ ). This suggests that for those with a history of depression, the presence of concurrent AD was associated with a greater likelihood of MDEs, whereas for those without a history of depression, the presence of concurrent AD was associated with a lower likelihood of MDEs. The 2-way interaction of the presence of concurrent AD and the presence of independent LLEs was not significant ( $p > .05$ ). The 3-way interaction was not significant ( $p > .05$ ). This suggests that the impact of independent LLEs does not depend on the presence of concurrent AD.

#### *Dependent SLEs*

*Lifetime AD.* At each time point, there was not a significant association between the presence of MDEs and the presence of dependent SLEs ( $p > .05$ ). At each time point, there also was not a significant association between the presence of MDEs and the presence of lifetime AD ( $p > .05$ ). However, there was a significant positive association between history of depression and the presence of MDEs at each time point ( $p < .01$ ).

The interaction of dependent SLEs and history of depression was not significant ( $p > .05$ ). The interaction of the presence of lifetime AD and history of depression was also not significant ( $p > .05$ ). However, the interaction of the presence of dependent SLEs and the presence of lifetime AD was significant ( $p < .01$ ). For those with lifetime AD, there was a significant positive association between the presence of dependent SLEs and

the presence of MDEs (estimate = .353;  $t = 3.32$ ;  $p = .00$ ). In contrast, for those without lifetime AD, there was a significant negative association between the presence of dependent SLEs and the presence of MDEs (estimate = -.290;  $t = -2.59$ ;  $p = .01$ ). This suggests that for those with a lifetime AD, the presence of dependent SLEs is associated with a higher likelihood of MDEs whereas for those without a lifetime AD, the presence of dependent SLEs is associated with a lower likelihood of MDEs. That is, the impact of dependent SLEs is greater in those with a lifetime AD as compared to those without a lifetime AD.

The 3-way interaction of the presence of lifetime AD, history of depression and the presence of dependent SLEs was significant ( $p < .01$ ). For those with lifetime AD, the interaction of history of depression and the presence of a dependent SLE was negative and significant (estimate = -.419;  $t = -3.77$ ;  $p = .00$ ). Specifically, for those with a lifetime AD and no history of depression, the association between the presence of a dependent SLE and MDE is positive and significant (estimate = .103;  $t = 3.05$ ;  $p = .00$ ). For those with a lifetime AD and a history of depression, the association between the presence of a dependent SLE and MDE is also positive and significant, but of greater magnitude (estimate = .143;  $t = 2.59$ ;  $p = .01$ ). This suggests that for those with a lifetime AD, the presence of dependent SLEs was associated with a higher likelihood of MDE: this association is stronger among individuals without a history of depression as compared to individuals with a history of depression.

For those without a lifetime AD, the interaction of history of depression and the presence of a dependent SLEs is positive and significant (estimate = .324;  $t = -2.64$ ;  $p = .01$ ). Specifically, for those without lifetime AD and no history of depression, the

association between the presence of a dependent SLE and MDE is negative and significant (estimate =  $-.452$ ;  $t = -2.66$ ;  $p = .00$ ). For those without lifetime AD and with a history of depression, the association between the presence of a dependent SLE and MDE is negative and significant, but of weaker magnitude (estimate =  $-.128$ ;  $t = -2.08$ ;  $p = .04$ ). This suggests that for those without a lifetime AD, the presence of dependent SLEs is associated with a lower likelihood of MDE, and this association is stronger among individuals without a history of depression as compared to individuals with a history of depression.

Taken together, the 3-way interaction suggests that for those without a lifetime AD, the impact of dependent SLEs is greater in individuals without a history of depression, supporting the SA model. However, for those with a lifetime AD, the impact of dependent SLEs is greater in individuals with a history of depression, supporting the SS model.

*Concurrent AD.* Similar to above, at each time point, there was not a significant association between the presence of MDEs and the presence of dependent SLEs ( $p > .05$ ). At each time point, there also was not a significant interaction between the presence of MDEs and the presence of concurrent AD ( $p > .05$ ). However, there was a significant positive association between history of depression and the presence of MDEs at each time point ( $p < .01$ ).

The interaction of dependent SLEs and history of depression was not significant ( $p > .05$ ). The interaction of the presence of concurrent AD and history of depression was significant ( $p < .05$ ). Specifically, for individuals with a history of depression, there was a significant positive association between the presence of concurrent AD and the presence

of MDEs (estimate = .288;  $t = 3.89$ ;  $p = .00$ ). However, for those without a history of depression, there was a significant negative association between the presence of concurrent AD and the presence of MDEs (estimate = -.360;  $t = -1.96$ ;  $p = .05$ ). This suggests that for individuals with a history of depression, there is a greater likelihood of MDEs when concurrent AD is present, whereas for individuals without a history of depression, there is a lower likelihood of MDEs when concurrent AD is present. In addition, the interaction of the presence of dependent SLEs and the presence of concurrent AD was significant ( $p < .01$ ). Specifically, for those with concurrent AD, there is a negative association between the presence of dependent SLEs and the presence of MDEs (estimate = -.067;  $t = -1.79$ ;  $p = .08$ ). However, for those without concurrent AD, there is a significant positive association between the presence of dependent SLEs and the presence of MDEs (estimate = .134;  $t = 3.57$ ;  $p = .00$ ). This suggests that for those with concurrent AD, dependent SLEs are associated with a lower likelihood of MDEs, whereas for those without concurrent AD, dependent SLEs are associated with a higher likelihood of MDEs. The 3-way interaction was not tested because all participants with concurrent AD and no history of depression did not have an event. Thus, the influence of concurrent AD on the impact of dependent SLEs as a function of depression history is unknown.

#### *Dependent LLEs*

*Lifetime AD.* At each time point, there was a significant negative association between the presence of dependent LLEs and the presence of MDEs ( $p < .01$ ). There was a positive association (significant at trend level) between history of depression and the

presence of MDEs at each time point ( $p = .06$ ). However, there was not a significant association between the presence of lifetime AD and the presence of MDEs ( $p > .05$ ).

The interaction between the presence of dependent LLEs and history of depression was not significant ( $p > .05$ ), indicating that the impact of dependent LLEs does not depend on history of depression. In addition, the interaction between the presence of dependent LLEs and the presence of lifetime AD was not significant ( $p > .05$ ). However, the interaction between the presence of lifetime AD and history of depression was significant ( $p < .05$ ). Specifically, for those with a history of depression, there was a positive association between the presence of lifetime AD and the presence of MDEs (estimate = .047;  $t = .41$ ;  $p = .69$ ). However, for those without a history of depression, there was a negative association between the presence of lifetime AD and the presence of MDEs (estimate = -.410;  $t = -1.29$ ;  $p = .20$ ). This suggests that for those with a history of depression the presence of lifetime AD is associated with a higher likelihood of MDEs whereas for those without a history of depression the presence of lifetime AD is associated with a lower likelihood of MDEs. The 3-way interaction of the presence of lifetime AD, history of depression, and the presence of dependent LLEs was not significant ( $p > .05$ ), indicating that the impact of dependent LLEs does not depend on the presence of lifetime AD.

*Concurrent AD.* At each time point, there was a significant negative association between the presence of dependent LLEs and the presence of MDEs ( $p < .01$ ). There was a positive association between history of depression and the presence of MDEs at each time point ( $p < .05$ ). However, there was not a significant association between the presence of concurrent AD and the presence of MDEs ( $p > .05$ ).

The interaction between the presence of dependent LLEs and history of depression was not significant ( $p > .05$ ), indicating that the impact of dependent LLEs does not depend on history of depression. In addition, the interaction between the presence of dependent LLEs and the presence of concurrent AD was not significant ( $p > .05$ ). However, the interaction between the presence of concurrent AD and history of depression was significant ( $p < .05$ ). For those with a history of depression, the association between the presence of concurrent AD and the presence of MDEs was positive (estimate = .240;  $t = 1.52$ ;  $p = .13$ ). In contrast, for those without a history of depression, the association between the presence of concurrent AD and the presence of MDEs was negative (estimate = -.588;  $t = -1.35$ ;  $p = .18$ ). This suggests that for those with a history of depression, the presence of concurrent AD is associated with a higher likelihood of MDEs whereas for those without a history of depression, the presence of concurrent AD is associated with a lower likelihood of MDEs.

The 3-way interaction of the presence of concurrent AD, history of depression, and the presence of dependent LLEs also was significant ( $p < .05$ ). For individuals without concurrent AD, the interaction of the presence of dependent LLEs and history of depression was not significant (estimate = .025;  $t = .27$ ;  $p = .79$ ). For individuals with concurrent AD, the interaction of the presence of dependent LLEs and history of depression was significant (estimate = -.210;  $t = -5.40$ ;  $p = .01$ ). Specifically, for individuals with concurrent AD and a history of depression, there was a significant negative association between the presence of dependent LLEs and MDEs (estimate = -.210;  $t = -5.40$ ;  $p = .00$ ). For individuals with concurrent AD and no history of depression,



there was not a significant association between the presence of dependent LLEs and MDEs (estimate = -.016;  $t = -.17$ ;  $p = .87$ ).

Taken together this suggests that for individuals without concurrent AD, the impact of dependent LLEs does not depend on history of depression. However, for those with concurrent AD, there is a stronger negative association between the presence of dependent LLEs and the presence of MDEs in those with a history of depression as compared to individuals without a history of depression. In other words, when concurrent AD is present, the impact of dependent LLEs is lower in individuals with a history of depression as compared to individuals without a history of depression, supporting the SA model.

#### *Occurrence*

See Table 14 for a summary of the analyses. The number of lines with AD present was 37 (18%) for the lifetime AD analyses and 12 (5.9%) for the concurrent AD analyses.

#### *Independent SLEs*

*Lifetime AD.* At each time point, there was a significant positive association between the presence of MDEs and the presence of independent SLEs ( $p < .05$ ). There was not a significant association between the presence of lifetime AD and the presence of independent SLEs ( $p > .05$ ). There also was not a significant association between the presence of history of depression and the presence of independent SLEs ( $p > .05$ ). The 2-way and 3-way interactions were not significant ( $ps > .05$ ). Taken together, this indicates that the occurrence of independent SLEs does not depend on the history of depression or the presence of lifetime AD.

*Concurrent AD.* Similar to above, at each time point, there was a significant positive association between the presence of MDEs and the presence of independent SLEs ( $p < .05$ ). However, there was not a significant association between the presence of concurrent AD and the presence of independent SLEs at each time point ( $p > .05$ ). There also was not a significant association between the presence of independent SLEs and the presence of history of depression ( $p > .05$ ). The 2-way interactions were not significant ( $ps > .05$ ), although the interaction of the presence of concurrent AD and the presence of MDE could not be tested because all participants with concurrent AD had an MDE. As a result, the 3-way interaction also was unable to be tested. Thus, it is unknown whether the occurrence of independent SLEs depends on the presence of concurrent AD. Taken together, results suggest that the occurrence of independent SLEs does not depend on the history of depression.

#### *Independent LLEs*

*Lifetime AD.* At each time point, there was not a significant association between the presence of MDEs and the presence of independent LLEs ( $p > .05$ ). At each time point, there also was not a significant association between the presence of independent LLEs and the presence of lifetime AD ( $p > .05$ ). There also was not a significant association between the presence of independent LLEs and the presence of history of depression ( $p > .05$ ). The 2-way and 3-way interactions were not significant ( $ps > .05$ ). Taken together, this indicates that the occurrence of independent LLEs does not depend on the history of depression or the presence of lifetime AD.

*Concurrent AD.* At each time point, there was not a significant association between the presence of MDEs and the presence of independent LLEs ( $p > .05$ ). At each

time point, there also was not a significant association between the presence of independent LLEs and the presence of concurrent AD ( $p > .05$ ). There also was not a significant association between the presence of independent LLEs and the presence of history of depression ( $p > .05$ ). The 2-way interactions were not significant ( $ps > .05$ ), although the interaction of the presence of concurrent AD and the presence of MDE could not be tested because all participants with concurrent AD had an MDE. As a result, the 3-way interaction also could not be tested. Thus, it is unknown whether the occurrence of independent LLEs depends on the presence of concurrent AD. Taken together, results suggest that the occurrence of independent LLEs does not depend on the history of depression.

#### *Dependent SLEs*

*Lifetime AD.* At each time point, there was a significant positive association between the presence of MDEs and the presence of dependent SLEs ( $p < .01$ ). However, there was not a significant association between each the presence of lifetime AD and the presence of dependent SLEs ( $p > .05$ ). There also was not a significant association between the presence of history of depression and the presence of dependent SLEs ( $p > .05$ ).

The interaction of the presence of MDE and history of MDE was significant ( $p < .05$ ). Specifically, for those with a history of depression there was a positive association between the presence of MDEs and the presence of dependent SLEs (estimate = .106;  $t = 1.61$ ;  $p = .11$ ). For those without a history of depression there also was a positive significant association between the presence of MDEs and the presence of dependent SLEs which was greater in magnitude (estimate = .382;  $t = 3.18$ ;  $p = .00$ ). This suggests

that the association between the presence of MDEs with prior dependent SLEs is stronger for first onsets than recurrences. In other words, the occurrence of dependent SLEs is greater for first onsets than recurrences, supporting both the SS and SA models. The other 2-way interactions and the 3-way interaction were not significant ( $p > .05$ ). Taken together, this indicates that the occurrence of dependent SLEs does not depend on the presence of lifetime AD.

*Concurrent AD.* At each time point, there was a significant positive association between the presence of MDEs and the presence of dependent SLEs ( $p < .01$ ). However, there was not a significant association between each the presence of concurrent AD and the presence of dependent SLEs ( $p > .05$ ). There also was not a significant association between the presence of history of depression and the presence of dependent SLEs ( $p > .05$ ).

Similar to above, the interaction of the presence of MDE and history of MDE was significant ( $p < .05$ ). Specifically, for those with a history of depression there was a significant positive association between the presence of MDEs and the presence of dependent SLEs (estimate = .165;  $t = 2.68$ ;  $p = .01$ ). For those without a history of depression there was also a positive significant association between the presence of MDEs and the presence of dependent SLEs which was greater in magnitude (estimate = .455;  $t = 3.89$ ;  $p = .00$ ). This suggests that the association between the presence of MDEs with prior dependent SLEs is stronger for first onsets than recurrences. In other words, the occurrence of dependent SLEs is greater for first onsets than recurrences, supporting both the SS and SA models.

The 2-way interactions were not significant ( $ps > .05$ ), although the interaction of the presence of concurrent AD and the presence of MDE could not be tested because all participants with concurrent AD had an MDE. As a result, the 3-way interaction also could not be tested. Thus, it is unknown whether the occurrence of dependent SLEs depends on the presence of concurrent AD.

#### *Dependent LLEs*

*Lifetime AD.* At each time point, there was not a significant association between the presence of MDEs and the presence of dependent LLEs ( $p > .05$ ). At each time point, there also was not a significant association between the presence of dependent LLEs and the presence of lifetime AD ( $p > .05$ ). There also was not a significant association between the presence of dependent LLEs and the presence of history of depression ( $p > .05$ ). The 2-way and 3-way interactions were not significant ( $ps > .05$ ). Taken together, this indicates that the occurrence of dependent LLEs does not depend on the history of depression or the presence of lifetime AD.

*Concurrent AD.* At each time point, there was not a significant association between the presence of MDEs and the presence of dependent LLEs ( $p > .05$ ). At each time point, there also was not a significant association between the presence of dependent LLEs and the presence of concurrent AD ( $p > .05$ ). There also was not a significant association between the presence of dependent LLEs and the presence of history of depression ( $p > .05$ ). The 2-way interactions were not significant ( $ps > .05$ ), although the interaction of the presence of concurrent AD and the presence of MDE could not be tested because all participants with concurrent AD had an MDE. As a result, the 3-way interaction also could not be tested. Thus, it is unknown whether the occurrence of

independent SLEs depends on the presence of concurrent AD. Taken together, results suggest that the occurrence of dependent LLEs does not depend on the history of depression.

## DISCUSSION

### Underlying Models of the Stress-Depression Relationship

#### *Cross-Sectional Analyses*

In the present study, we compared the underlying models proposed to explain the stress-depression association in a community sample of young adult women experiencing first onsets versus recurrences of depression. This is the first study to directly target both the impact and occurrence of life events in order to elucidate the underlying models of the association, deemed to be essential by experts in the field (Hammen, 2005; Monroe & Harkness, 2005). Overall, analyses revealed some support for the SS model over the SA model: the impact of independent SLEs and LLEs was greater in recurrences than first onsets, providing evidence that individuals may become sensitized to stress with successive recurrences. In addition, consistent with both models, the occurrence of dependent SLEs was greater in first onsets than recurrences, suggesting that these events are less likely to be present prior to recurrences.

#### *Changes in the Impact and Occurrence of SLEs in First Onsets versus Recurrences*

Two main findings emerged from the analyses investigating the role of SLEs: (1) dependent, but not independent, SLEs were less likely to be present prior to recurrences (decrease in occurrence); and (2) independent, but not dependent, SLEs had a greater impact for recurrences than first onsets. This suggests that with successive recurrences, there are changes in the occurrence of dependent SLEs and changes in the impact of independent SLEs. As discussed, previous research on SLEs has demonstrated a decline in the strength of the stress-depression association with successive recurrences (e.g., Kendler et al., 2000). However, this work does not illuminate if the decline in strength is

due to a decrease in the occurrence or impact or both (Monroe & Harkness, 2005). Taken together, the current findings suggest that the decline in the association evidenced in previous research may be due to changes in impact and occurrence, depending on the independence of the SLE.

It is difficult to make comparisons to other work, as most studies have not distinguished between the impact and occurrence of SLEs. The one study that has specifically examined occurrence, however, produced findings that are very consistent with those of the present study. Monroe and colleagues (2007) demonstrated that severe dependent (but not independent) events were less likely to be present prior to episodes, as episode number increased. Specifically, 50% of individuals experiencing first onsets and 39% of individuals experiencing first recurrences had a prior SLE (Monroe et al., 2007). Although the authors did not target the impact of SLEs, the authors hypothesized that SLEs retained their capacity to trigger episodes, but were less likely to be present. Our findings reinforce and extend their prediction. That is, it appears that dependent SLEs do retain their capacity to trigger episodes, as their impact was not significantly different for first onsets and recurrences. However, independent SLEs increased in their impact to trigger recurrences (discussed below).

#### *Changes in the Impact and Occurrence of LLEs in First Onsets versus Recurrences*

The impact of independent, but not dependent LLEs, was greater in recurrences than first onsets. The occurrence of both independent and dependent LLEs, however, remained the same for first onsets and recurrences. Taken together, these results suggests one mechanism by which the stress-depression association changes over time is by the increasing impact of independent LLEs, via stress sensitization, without accompanying



changes in the extent to which LLEs are present prior to episodes. This extends other work on the role of LLEs, which cannot ascertain if LLEs more strongly predict recurrences than first onsets because of changes in impact or occurrence or both (e.g., Harkness & Monroe, 2006; Monroe et al., 1996; Monroe et al., 2006, Ormel et al., 2001). Thus, our findings add to a growing body of literature supporting the importance of LLEs for recurrences of depression and stress sensitization as a mechanism of change in the stress-depression association.

The present findings are consistent with the notion that only certain types of LLEs may be relevant for recurrences of depression (Monroe et al., 2006). Monroe and colleagues (2006) showed that the role of LLEs in predicting recurrences was limited to independent events. In addition, this effect was limited to participant-focused events and medicated patients, with the absence of LLEs associated with recurrence among non-medicated patients (Monroe et al, 2006). However, Lenze and colleagues (2008) demonstrated that “nonindependent” (dependent) LLEs that were participant- or joint-focused (focused on the participant and another person) significantly predicted time to recurrence in patients receiving psychotherapy alone. It is likely that the differences in independence were due to differences in methods. Our methods are more similar to Monroe and colleagues who examined the likelihood of recurrence in a 6-week period following the presence of an LLE. That is, for impact, we examined the conditional probability of first onsets and recurrences within 3 months of experiencing an LLE. Lenze and colleagues examined LLEs occurring over a 2-year period, examining the increased risk incurred with each additional LLE. Thus, it may be the case that independent LLEs are salient in the period most proximal to recurrences, whereas when

longer periods are examined, dependent LLEs are salient, the latter of which is consistent with research on stress generation (e.g., Harkness, Monroe, Simons & Thase, 1999; discussed further below).<sup>2</sup> It is also important to note that the current results extend the generalizability of both sets of findings based on highly recurrent patient samples who recovered from treatment with interpersonal therapy (in combination with pharmacotherapy in some cases) to a community sample of young women whom likely have experienced fewer recurrences. As discussed, a focus on fewer recurrences is preferred given that changes in the stress-depression association are likely to begin with the first recurrence, and stress processes may be more difficult to detect in later recurrences (Monroe & Harkness, 2005).

#### *Changes in Impact were Specific to Independent Events*

It is worth speculating why independent, but not dependent, SLEs and LLEs had more impact for individuals with a history of depression than for those without a history. Most generally, it is consistent with other work that shows that independent SLEs are important for triggering both first onsets and recurrences (e.g., Shrout et al., 1989). Our findings extend this by suggesting that independent SLEs continue to predict episodes of depression via increases in impact.

In order to more fully understand this finding, I examined the types of independent SLEs and LLEs that were followed by recurrences. Example of SLEs included: 5-year old cousin died, friend died, father died and aunt made a suicide attempt. Examples of LLEs included: found out ex-boyfriend was getting married, father arrested, grandfather died, mother went to Iran for business, dated someone three times and he stopped calling, and grandmother ill. Interestingly, most of these events were

uncontrollable losses (e.g., loss of a person, role, resources or a cherished idea, or a disappointment; e.g., Brown, Harris & Hepworth, 1995) in close interpersonal relationships. This aligns with extensive research documenting the role of independent loss events in depression (e.g., Brown, 1993). For example, in Brown & Harris' (1978) classic study of stress and depression in women, 79-88% of the severe events that occurred prior to episodes were loss events. It is also consonant with attachment theory's focus on the role of loss events in increasing vulnerability to depression. Specifically, Bowlby (1980) asserts that early experiences with loss or separation have lasting effects on subsequent responses to loss and separation, such that attachment mediates the association between early loss and perceptions of subsequent losses. Thus, early losses and separations led to the development of models of relationships and of others, which affect how subsequent losses are perceived. Bowlby maintains that early loss involving death (usually an independent event by nature) leads individuals to respond to subsequent losses with hopelessness and depression. This suggests that loss and the consequences of loss on attachment and views of self and relationships may set the stage to respond to subsequent losses with depression. Although loss here is not restricted to early loss, Bowlby's theory aligns with the idea that experiences with loss may have cognitive consequences (and neurological consequences in stress sensitization) that render subsequent losses more depressogenic.

Further, the uncontrollable nature of these events is consistent with the role of helplessness in depression (e.g. Abramson, Metalsky, & Alloy, 1989; Seligman, 1975) which has been documented extensively in the literature. For example, research suggests that loss events are more likely to be followed by depression at lower levels of control.

Brown et al. (1995) showed that about 50% of individuals became depressed following loss with the least control, about 25% after loss with some control, and about 10% after a loss with the most control (e.g., a separation initiated by the person). Thus, it appears that the independence of the event plays a key role in increasing the potency of loss events.

Several directions for future research stem from this finding. First, the role of perceived uncontrollability is unknown, as the objective independence of events was coded. As discussed, perceived uncontrollability may function to increase feelings of helplessness in the presence of life events (Alloy et al., 1990; Mineka et al., 1998), leading to their increased impact. Thus, investigating changes in impact according to objective versus subjective levels of controllability is of interest (see also Monroe, 2008). Second, there is a body of work documenting the association between childhood adversity, including loss events, and stress sensitization (e.g., Hammen et al., 2000), but we do not yet know if early loss events differentially sensitize individuals to loss events or events in general (Slavich, Monroe & Gotlib, 2009). This idea is also implied by Post (1992) in his formulation of the kindling/sensitization hypothesis. He stated: loss events “may have very different cognitive, behavioral, and neurobiological consequences” than threat events, but these syndromes likely involve some of the same “mechanisms” (p. 1004). Thus, in the present study, it could be the case that it is only participants with early loss who demonstrate increased likelihood of depression following loss events. As such, research examining sensitization to specific types of events, particularly loss events, is a promising area of future research. Third, given the current sample is composed of women, it will be important to determine the generalizability of these findings to men. We did not formally code events according to focus, but as can be seen in the examples of LLEs

followed by recurrences, events that were focused on the participant herself or joint focused (the participant and a person with whom the participant is in a close relationship) were followed by recurrences. As discussed, only participant-focused events predicted recurrences in one study where the sample was approximately 75% female (Monroe et al., 2006) whereas participant and joint focused events predicted recurrences in a second study where the sample was also 100% female (Lenze et al., 2008). Although there are other differences between these studies and the current study (discussed previously), it is possible that joint focused LLEs may only be associated with recurrences for women. Although there are exceptions, research indicates that women may be more sensitive or reactive to certain events, especially interpersonal ones (e.g., Kessler & McLeod, 1984; Maciejewski, Prigerson, & Mazure, 2001; Nazroo, Edwards, & Brown, 1997) as well as more attuned to and involved in things occurring in the interpersonal domain of their lives (Feingold, 1994). As such, joint focused events may increase in impact for women, but not men. Thus, more work is needed to replicate the finding that changes in impact of SLEs (and LLEs, discussed below) are specific to independent events in both men and women.

#### *Stress Generation and Stress Sensitization*

Another important question is whether the occurrence findings are inconsistent with stress generation (Hammen, 1991). We found that the occurrence of dependent SLEs was greater in first onsets than recurrences and the occurrence of dependent LLEs remained constant. At first glance, it may appear this is inconsistent with stress generation, which predicts elevated rates of dependent life events in individuals with a history of depression (see Hammen, 2006 for a review). However, here we define

occurrence as the conditional probability of an event (SLE or LLE) within 3 months prior to the presence of an MDE, and we are comparing individuals experiencing first onsets versus recurrences. In contrast, most research on stress generation has compared those with a history of depression to those with no disorder (e.g., Hammen, 1991; not first onsets versus recurrences), and in most cases, the time interval investigated is longer (e.g., 12 months), and therefore, not directly prior to episodes. In fact, consistent with the present study, in their examination of stress generation in first onsets versus recurrences, Harkness and colleagues (1999) demonstrated that the individuals experiencing first onsets and recurrences did not differ in the number of dependent life events (severe and nonsevere) or the presence of dependent SLEs in the 3 months prior to episodes. However, as compared to individuals experiencing first onsets, individuals experiencing recurrences experienced significantly more dependent life events in the 12 months before onset (Harkness et al., 1999). Thus, as suggested by the authors, it may be the case that the generation of dependent events does not lead to recurrences specifically, but rather to an increase in the number of events experienced overall by individuals with a history of depression, and thus, our results would not be inconsistent with stress generation. In addition, the interview used in the current study does not assess the full range of stressors, rendering it possible that the occurrence of more minor daily stressors (not assessed with traditional life stress interviews; see Monroe & Harkness, 2005) increases over the course of the disorder (see Hazel & Hammen, 2009), when LLEs do not. This would be consistent with stress-generation, but unfortunately, with the methods used in the present study, our conclusions are limited to SLEs and LLEs. Of note, Monroe and colleagues (2007) have suggested that the processes of stress generation and stress sensitization may

be mutually reinforcing, based on their results showing that the role of SLEs decreased and the role of chronic stress increased from first onsets to recurrences. Thus, our results do not eliminate the possibility that both processes may occur together.

### *Limitations*

One of the main questions raised by the current findings is how (and if) the mechanisms of stress sensitization (and stress autonomy) may evolve with successive recurrences. Because of their cross-sectional nature, the current findings provide only a snap shot of how the role of stress changes over time, comparing first onsets to recurrences, at different numbers of recurrences. Thus, it is possible that longitudinal within-person analyses may reveal changes that provide greater consistency with the SS model (such as increases in the occurrence of LLEs) or not (discussed below).

### *Summary*

Taken together, the current results suggest that stress sensitization may be the primary mechanism of change in the stress-depression association over time. This adds to a large body of work supporting the stress sensitization perspective (e.g., Monroe et al., 2006, 2007), and extends it by highlighting specific changes in the impact and occurrence of both SLEs and LLEs that are consistent with the SS model. However, the results also suggest that the impact and occurrence of certain events do not change with successive recurrences. This suggests that we need to move beyond the notion that the stress-depression changes to address not only how it changes (Monroe, 2008), but for what types of events.

## *Longitudinal Within-Person Analyses*

### *Overview*

To further understand changes in the role of life events as well as avoid the methodological disadvantages of cross-sectional designs, I also examined the role of SLEs and LLEs using longitudinal within-person analyses. This extends other longitudinal work that has greatly contributed to the field, but cannot discriminate between the models (Kendler et al., 2000, 2001). (Hammen, 2005; Monroe & Harkness, 2005). In addition, there is evidence that other factors influence stress sensitization, including early adversity (e.g., Harkness, Bruce & Lumley, 2006), pubertal stage (Rudolph & Flynn, 2007) and genetic risk (e.g., Kendler et al., 2005), before the first episode of depression (Kendler, Thornton & Gardner, 2001). Thus, longitudinal within-person analyses eliminate the possibility that systematic differences between the first onset and recurrence groups (particularly in factors shown to influence sensitization) are driving the results. This is the first study to investigate changes in the impact and occurrence of SLEs and LLEs using longitudinal analyses, thereby elucidating the underlying models of the stress-depression association.

Unfortunately, results yielded changes in impact and occurrence that were not entirely consistent with the cross-sectional analyses. For SLEs results indicated: (1) the impact of independent and dependent SLEs did not depend on history of depression; but (2) the occurrence of dependent, but not independent, SLEs was greater in first onsets than recurrences of depression. For LLEs results indicated: (1) the impact of dependent, but not independent LLEs, varied as a function of depression history; but (2) the occurrence of dependent and independent LLEs did not change.

*The Occurrence of Dependent SLEs Decreased with Successive Episodes*



Both the cross-sectional and longitudinal analyses revealed decreases in the occurrence of dependent SLEs, with no other events showing decreases in occurrence. That is, dependent SLEs are less and less likely to be present prior to MDEs with successive episodes. As discussed, this finding does not allow us to discriminate between the underlying models of the stress-depression association as both models predict a decrease. The SS model predicts that the occurrence of SLEs decreases, because as individuals become sensitized to stress, events of lower severity are more likely to be present prior to episodes. The SA model predicts decreases in the occurrence of SLEs because episodes begin to arise independently of stress (Monroe & Harkness, 2005). Although this finding does not discriminate between the models, it does align with the two previous longitudinal studies demonstrating a decline in the strength of the association between SLEs and depression with successive episodes (Kendler et al., 2000, 2001). As mentioned, these previous studies did not investigate changes in impact and occurrence, and thus do not elucidate how the association changes over time. Extending that work, the current findings suggest that the decline evidenced in those studies was likely due to a decline in the occurrence of dependent SLEs and not due to a decline in their impact. In addition, it is consonant with recent cross-sectional research demonstrating a decline in the occurrence of dependent SLEs as a function episode number (Monroe et al., 2007). In both studies, the decrease in occurrence of SLEs was specific to dependent SLEs. Thus, evidence is beginning to emerge in support of a decreasing occurrence of dependent SLEs with successive episodes.

In spite of the emerging consistency, it is important to note that there are limitations in the present sample that could substantially influence the results. In

particular, very few individuals experienced a first onset and a recurrence during the study period (e.g.,  $n = 17$  in the longitudinal occurrence analyses), even less experienced more than 3 episodes including a first onset (e.g.,  $n = 12$  in the longitudinal occurrence analyses), with the majority of individuals experiencing only 1 episode during the study. Of those, that experienced multiple episodes, these were mostly recurrences (i.e., not paired with a first onset). Although we can speculate that these are earlier recurrences because of the young age of the sample, we do not know the episode number for those that entered the study with a history of depression. Thus, results indicated a decline in the occurrence of dependent SLEs, but conservatively, we can only conclude there is a decline with successive episodes, not that there is a decline from first onsets to recurrences. To provide a true test of the models, we need to capture first onsets and early recurrences in the same individuals.

#### *The Impact of Dependent LLEs Decreased with Successive Episodes*

In contrast to the cross-sectional analyses, results suggested that the impact of dependent LLEs decreased with successive episodes of depression. This finding aligns with the SA model which asserts that events will become progressively less potent, as episodes begin to arise independently of stress (Monroe & Harkness, 2005). The model holds that major life stress and episodes of depression contribute to the development of other processes with successive episodes, such that these processes develop the capacity to bring about episodes independently of psychosocial factors. Further, the model maintains that there will be an initial spike in sensitization, followed by a progressive independence of episodes from stress. As discussed by others, this model is less parsimonious, as the alternative processes and the switch to independence must be

explained. At the present time, both of these areas are poorly understood (Monroe & Harkness, 2005). It is important to note that the studies evidencing a decline in the strength of the stress-depression association investigate SLEs, not LLEs (e.g., Kendler et al., 2000) and thus, this finding does not speak to why previous studies evidenced a decline in the association.

Overall, this finding is inconsistent with other research on the role of LLEs. As discussed, several studies have shown that LLEs predicted recurrences (Harkness & Monroe, 2006; Lenze et al., 2008; Monroe et al., 1996; Monroe et al., 2006, Ormel et al., 2001). Although these studies do not directly examine the impact of LLEs, they do suggest that the role of LLEs is greater in recurrences as compared to first onsets. In terms of independence, this finding does partially align with research indicating that dependent LLEs did not predict recurrences of depression (Monroe et al., 2006). However, it is inconsistent with recent work demonstrating the cumulative impact of dependent, not independent, LLEs in predicting recurrences (Lenze et al., 2008).

This finding also contradicts the cross-sectional findings which indicated that the impact of independent events increased, supporting the SS model. Thus, one interpretation of the present finding is that independence is crucial in understanding how the impact of events changes as a function of depression history. That is, uncontrollable non-severe events may increase in their impact, but dependent non-severe events may lose potency over time. Another important consideration in interpreting these findings is the elevated frequency of dependent LLEs in comparison to the other types of events. Thus, it is possible that because these events are so frequent, their impact diminishes with the course of depression. Related to their frequency is the notion that the class of

dependent severe events needs to be refined in order to find consistent effects, a point advocated by others in relation to the total class of non-severe events (Monroe et al., 2006). Thus, it may be the case that these events differ in their effect on depression, if the events are classified more specifically. Examples of dependent non-severe events include relationship break-ups, moves, car accidents, failed exams, part-time job loss, dating for the first time after a significant break-up, starting a new job, and transferring universities. The heterogeneity of the class of dependent non-severe events is highlighted by this list. Therefore, the potency of different types of events may vary, with some increasing in impact and others decreasing. As such, future work should aim to continue to refine the class of non-severe events, developing more specific categories than independence (discussed further below). Another point underscored by the elevated frequency of dependent LLEs is that because these events were more frequent, there was more power to detect effects in these analyses. The lack of changes evidenced in the impact of other events in these analyses may be due to their lower frequencies.

#### *Few Changes Evidenced in the Role of Stress with Successive Recurrences*

The impact and occurrence of most events did not change with successive episodes in the longitudinal analyses. This does not support Post's model. It is not clear why the changes in the impact of independent SLEs and LLEs did not replicate in these analyses. One possibility is that the low frequency of independent events (as compared to dependent events) reduced the power to detect changes in these events, especially in detecting interactions. In addition, as mentioned, there was a low frequency of first onsets and first recurrences in the same individuals, and instead, when multiple episodes occurred in the same individual, it was likely multiple recurrences (rather than a first

onset with successive recurrences). As a result, it could be the case that the changes in impact of independent events occur early in the course of the disorder, and thus, the changes had already occurred prior to the recurrences included in the analyses. Consistent with this, Monroe and Harknesss (2005) asserted than changes in the association will likely occur early in the course of the disorder, even between the first onset and first recurrence, and as a result, it will be difficult to detect changes among later recurrences. Thus, if this interpretation were true, the lack of changes in impact for independent events would reflect that most individuals were already sensitized to stress, reaching a peak of sensitization or a point where there is little change between episodes. Unfortunately, there is not research on impact that tests this assertion, but we do have some evidence (not specific to impact or occurrence) that the association between severe events and depression changes after the first episode (e.g., Kendler et al., 2000, 2001; Ormel et al., 2001).

Alternatively, it could be the case that the increase in impact evidenced in the cross-sectional analyses reflected the predicted early spike in sensitization, that is followed by an insensitivity to stressors in the SA model, rather than changes consistent with the SS model (Monroe & Harkness, 2005). However, the SA model predicts a decline in the impact of events following the spike, which was not consistent with the current findings. Instead, there was no change in the impact of independent events with successive episodes. Thus, this explanation is possible, but unlikely.

A third possibility is that other between group differences were driving the cross-sectional findings, which were eliminated in the longitudinal analyses. For example, it could be the case that the recurrence group was sensitized to stress via early childhood

adversity (e.g., Hammen et al., 2000) or genetic risk (e.g., Caspi et al., 2003) before the first episode of depression such that the experience of depression did not contribute to their increased risk of MDEs following independent events. All of these notions underscore the need for research examining first onsets and first recurrences in the same individuals (Hammen, 2005; Monroe & Harkness, 2005).

### *Summary*

In spite of the limitations of these analyses, it is also important to consider that the impact and occurrence of all types of events may not change even when the methods are ideal. Thus, we need to continue to refine our understanding of the stress-depression association by examining changes in the roles of specific types of events among early episodes of depression (see also Monroe et al., 2006; Monroe & Harkness, 2005).

### The Influence of Comorbid Anxiety on the Stress-Depression Association

#### *Cross-Sectional Analyses*

Overall, in contrast to my predictions, the cross-sectional analyses suggested that there was no evidence that the presence of a lifetime history of at least one AD influenced the stress-depression association. Thus, based on these analyses, it does not appear that anxiety presensitizes or prekindles individuals to stress before the first episode of depression. This is in contrast to recent work indicating that the presence of anxiety increases sensitization to stress in the context of childhood adversity (Espejo et al., 2006). Other work offers little comparison, as this idea is novel.

If anxiety does in fact influence the stress-depression association, it is probably the case that the low incidence of anxiety disorders greatly limited the power to detect its influence. In some cases only one participant had an AD in the analysis and overall, less

than 15% of the sample had an AD (see also Table 8). In addition, in order to find an effect for anxiety, the interaction had to be significant, further increasing the incidence of ADs needed to find an effect. Also, because participants were only included in the occurrence analyses if they experienced an MDE ( $n = 70$ ) or the target event in the impact analyses ( $n = 103-149$ ), the number of participants included in the analyses was lower than the total number of participants in the study. All these factors likely substantially reduced the power to find effects.

In some cases, the presence of lifetime AD before the target event or MDE was associated with greater likelihood of a history of depression. This is consistent with a large body of research evidencing greater comorbidity of anxiety and depression in individuals with recurrent depression (Wilhelm et al., 1999). However, it is not related directly to the study hypotheses.

Notably, the finding that the impact of independent SLEs and LLEs is greater in individuals with a history of depression was replicated using logistic regression. This boosts our confidence that this finding will be replicated in other work, at least cross-sectionally, for women. These analyses also control for the effect of anxiety; thus, we find evidence for the enhanced impact of independent events, even after taking into account anxiety. However, we did not replicate finding that the occurrence of dependent SLEs is greater in first onsets than recurrences. As mentioned above, this may have been because of the low number of participants included in the occurrence analyses as compared to the impact analyses, especially given this finding was replicated longitudinally. Nonetheless, these inconsistencies point to the need to replicate these findings in future research.

In sum, the limitations of the current dataset may account for the lack of influence of anxiety on the stress-depression association. It is important to point this out as to not discourage research on this important area of research, as there is a large body of evidence to suggest that anxiety does impact the association.

#### *Longitudinal Within-Person Analyses*

Overall, similar to the cross-sectional analyses, there was no evidence that a history of anxiety disorders presensitizes or prekindles individuals to stress as I predicted. However, in contrast to the longitudinal analyses, there was some evidence that the presence of a lifetime history of at least one AD or concurrent AD influenced the stress-depression association.

#### *Comorbid Anxiety Affects the Impact of Life Events*

Even though the predicted influence of anxiety was not supported, there was evidence that the presence of anxiety influences the stress-depression association. In terms of the impact of events, 3 main findings emerged: (1) the impact of dependent SLEs depends on both history of depression and the presence pre-existing anxiety; (2) the impact of dependent LLEs depends on both history of depression and the presence of co-occurring anxiety; and (3) the impact of independent SLEs and dependent SLEs depends on the presence of co-occurring anxiety. Before describing the results, it is important to consider that these findings are based on a very small number of participants with anxiety disorders and thus, the findings are tentative. Replication with a larger sample is needed, before drawing conclusions from these results.

*The impact of dependent SLEs depends on the presence of pre-existing anxiety and history of depression.* Results indicated that for those without a pre-existing AD, the



impact of dependent SLEs was greater in those without a history of depression, supporting the SA model. In contrast, for those with at least one pre-existing AD, the impact of dependent SLEs was greater in those with a history of depression, supporting the SS model. Interestingly, this finding suggests that one reason the other analyses, both cross-sectional and longitudinal, did not evidence changes in the impact of dependent SLEs with successive recurrences may be because pre-existing anxiety was not accounted for. In addition, regardless of history of depression, the impact of dependent SLEs was greater in those with pre-existing anxiety as compared to those without pre-existing anxiety.

Taken together, these findings suggest that pre-existing anxiety may increase the impact of life events, and that in those with a history of anxiety, the impact of dependent SLEs may continue to increase with successive episodes of depression. As discussed, there are several potential ways that pre-existing anxiety may serve to increase the impact of events. First, the processes of sensitization have been implicated in a variety of anxiety disorders (e.g., Post & Weiss, 1998) and rates of life events are elevated prior to the development of anxiety disorders (e.g., Servant et al., 1991). Thus, it is possible that individuals are sensitized to stress in the context of anxiety. This is consistent with recent research on the association between early childhood adversity and increased vulnerability to low levels of stress, reflecting stress sensitization. Specifically, a history of anxiety disorders enhanced sensitization to stressors as a function of childhood adversity: among youth who had a high degree of childhood adversity, those with a history of anxiety showed more severe levels of depression in the face of low stress as compared to youth without a history of anxiety. Unexpectedly, the same effect was not found at high levels

of stress (Espejo et al., 2006). In comparing these findings to the present study, it is important to note that the authors examined the total objective impact of all events that occurred in a one year period, and thus, it is not clear if severe and/or non-severe events contributed to the stress rating. In addition, the total stress ratings were for the one year period prior to the interview, and therefore, not necessarily reflective of stress occurring before the onset of symptoms. In addition, Espejo and colleagues examined the severity of symptoms, rather than the presence or absence of episodes. Thus, the current findings extend those results by suggesting that anxiety may contribute to increased impact of dependent SLEs, occurring before episodes of depression. In addition, the current findings suggest that a history of anxiety may sensitize individuals to stress outside the context of childhood adversity.

Second, the sensitization effect may be mediated by alterations in the biological stress mechanisms, such as the hypothalamic-pituitary-adrenal (HPA) axis (as discussed by Heim & Nemeroff, 2001 in the case of early adversity). Some research indicates that alterations in the HPA axis are prominent in depression and anxiety disorders. In fact, research demonstrated that those with comorbid anxiety and depression exhibited HPA dysregulation in responding to a social stressor, whereas those with pure depression and pure anxiety did not (Young, Abelson, & Cameron, 2004) This is important because alterations in the HPA axis may lead to heightened reactivity to stress (Heim & Nemeroff, 2001). Thus, comorbid individuals, in particular, may show alterations in HPA functioning, leading to enhanced impact of life events.<sup>3</sup>

Third, events may have more impact in those with pre-existing anxiety due to increased feelings of helplessness in the face of events. Specifically, past experiences of

uncontrollability and helplessness occurring in the context of anxiety may function to increase feelings of helplessness in the presence of life events (Alloy et al., 1990; Mineka, Watson & Clark, 1998), leading to their increased impact. Interestingly, impact increased for dependent SLEs, events in which the participants had some control over their occurrence. However, as discussed independence was coded by an objective rating team, and thus, events are not rated by participants according to perceived controllability of the event. Thus, one possibility is that even though the events were in partial control of the participant, individuals with pre-existing anxiety were more likely to perceive the event as uncontrollable, thereby increasing its' impact. However, individuals without pre-existing anxiety may more perceive the event to be at least partially controllable, decreasing its' impact. Future research should examine the correlation between objective and subjective ratings of independence in relation to the objective impact of life events.

Thus, there are several ways in which pre-existing anxiety may contribute to stress sensitization. However, it is important to note that we did not measure childhood adversity or other factors known to contribute to sensitization to stressors. Thus, we cannot rule out the possibility that the group with a history of anxiety disorders was sensitized to stress via other factors, such as childhood adversity (e.g., Hammen et al., 2000) or genetic factors (e.g., Kendler et al., 2001). That is, anxiety itself may not have contributed to increased vulnerability to stressors. Instead, it may reflect sensitization that occurred prior to the development of anxiety. This idea is indirectly supported by combining a few lines of research. Research indicates that anxiety disorders may be more strongly related to early adversity as compared to depression (Phillips, Hammen, Brennan, Najman & Bor, 2005). In addition, as discussed, early adversity has been linked to

alterations in biological stress mechanisms, specifically, in the HPA axis, rendering individuals more vulnerable to depression in the face of subsequent stress (e.g., Heim & Nemeroff, 2001). Thus, for those with pre-existing anxiety, one possible pathway to sensitization (prior to a first onset of MDE) is that childhood adversity led to abnormal HPA functioning, potentially leading to anxiety disorders (reflecting and causing further sensitization), and finally, to depression (e.g., as proposed by Espejo et al., 2006). Our results suggest that the process of sensitization may continue beyond a first onset, with those with pre-existing anxiety becoming increasingly vulnerable to dependent SLEs. Therefore, we cannot discount the possibility that those with pre-existing anxiety disorder may have been sensitized to stress via other avenues, independent of anxiety.

It is interesting to consider how the processes of stress generation and stress sensitization may compliment each other in individuals with a history of anxiety. Research on stress generation and comorbidity suggests that individuals with co-occurring anxiety and depression may experience higher levels of dependent life stress (Daley et al., 1997). In addition, other work suggests that individuals with comorbid dysthymia and anxiety experience higher rates of dependent events prior to episode onset (Harkness & Luther, 2001). Even though this research examined co-occurring anxiety and not necessarily lifetime history of anxiety, it does suggest that the process of stress generation may be enhanced by comorbid anxiety. If individuals with a pre-existing anxiety disorder are also sensitized to stress, showing increased vulnerability to dependent SLEs, then not only are these individuals potentially generating elevated rates of dependent events, but they also may be more vulnerable to depression in the face of these events. This effect also may escalate with the course of depression, as research on

stress generation suggests it may be progressive, with higher rates of events generated by those with recurrences as compared to those with first onsets (Harkness et al., 1999), coupled with the current finding which demonstrates enhanced sensitization with successive episodes.

One question raised by the current findings is why the impact of dependent SLEs decreased with successive episodes in individuals without a pre-existing anxiety disorder. This finding is difficult to explain, given the SA model asserts that other processes develop that begin to initiate episodes independently of stress, and such processes are not well understood (Monroe & Harkness, 2005). In this regard, there is not existing research supporting the SA model, whereas there is now building evidence for the SS model (e.g., Monroe et al., 2006, 2007). One could argue that existing research on the stress-depression association has supported the SS model because participants had a lifetime history of anxiety disorders. This is supported by the high rates of comorbidity between depression and anxiety (Kessler et al., 1994), the infrequency of pure depression (Alloy et al., 1990), and the tendency for anxiety to precipitate MDD, rather than the reverse (Kessler et al., 1996). However, given existing research has evidenced support for the SS model with severe and non-severe events (Monroe et al., 2006, 2007), has not examined the impact of events outside of the context of childhood adversity, and the sensitization effect was not replicated in other types of events, this is unlikely.

*The impact of dependent LLEs depends on the presence of co-occurring anxiety and history of depression.* Results suggested that for those without a co-occurring AD, the impact of dependent LLEs does not depend on history of depression. That is, Post's model is not supported among those without a co-occurring AD. But, for those with a co-

occurring AD, the impact of dependent LLEs is lower in those with a history of depression, supporting the SA model. That is, in direct contrast to the influence of pre-existing anxiety on the impact of dependent SLEs: among those with co-occurring AD, dependent LLEs are less likely to be followed by MDEs with successive recurrences.

This suggests that when anxiety is present, non-severe dependent events have less impact (although their occurrence appears to remain constant, see below) with successive episodes. As mentioned, this aligns with the SA model which asserts that events will become progressively less potent, as episodes begin to arise independently of stress (Monroe & Harkness, 2005). The model holds that major life stress and episodes of depression contribute to the development of other processes with successive episodes, such that these processes develop the capacity to bring about episodes independently of psychosocial factors. At the present time the exact processes as well as when in the course of depression these processes take over and begin triggering episodes is unknown (Monroe & Harkness, 2005). Thus, one possible interpretation of the current findings is that co-occurring anxiety serves to initiate these other processes. That is, because both kindling (SA) and sensitization (SS) processes have been implicated in anxiety disorders (e.g., Post & Weiss, 1998), it is possible that anxiety may have kindled individuals to stress (in the same way we discussed above for sensitization), with the processes continuing to develop with successive recurrences. However, the current finding is for co-occurring anxiety; although most participants had anxiety at some point in the past. Alternatively, it could be the case that anxiety itself gives rise to episodes of depression, or that there are different pathways to depression, not involving life stress, when anxiety is present. This is supported loosely by research demonstrating that co-occurring anxiety

predicts recurrences of depression (O’Leary et al., 2000), but this research does not indicate how or if recurrences may be initiated differently when co-occurring anxiety is present.

Not only is this finding difficult to explain, it is difficult to reconcile with the literature and it contradicts the other arguments and research presented in this discussion, which suggest that anxiety increases the impact of life events. Given its inconsistency, one possibility is that because there were so few individuals with co-occurring AD in these analyses (12 people with a total of 19 lines out of total of 783 lines), this finding is an anomaly and is unlikely to be replicated.

*The impact of dependent and independent SLEs depends on the presence of co-occurring anxiety.* Consistent with the effect of co-occurring anxiety on dependent LLEs, dependent SLEs and independent SLEs had a greater impact among those without co-occurring anxiety as compared to those with co-occurring anxiety. That is, SLEs are less likely to be followed by MDEs when co-occurring anxiety is present. Unfortunately, both of the 3-way interactions were not testable, and therefore, we do not know if these associations depend on a history of depression.

As discussed in relation to dependent LLEs, these findings are inconsistent with the idea that anxiety may increase the impact of life events; instead, it appears that anxiety increases the impact of SLEs. Further, these findings suggest that there may be other pathways to depression, independent of life stress, when anxiety is present. However, research demonstrates that severe events continue to be of etiological importance for depression, even with multiple recurrences (e.g., Monroe et al., 2007). Thus, rather than supporting pathways independent of severe life stress, research has highlighted their

continued significance for depression. Because it is inconsistent with what we know about the relation of major stress and depression, replication is clearly needed.

In sum, it appears that co-occurring anxiety decreases the impact of severe events and dependent LLEs (discussed above). Not only are these findings difficult to explain, it is difficult to reconcile them with existing research. Given this and the very low incidence of co-occurring anxiety in the present study, these findings should be interpreted with caution. In addition, although results suggested that co-occurring anxiety does not affect the impact of independent non-severe events, these events were the least frequent of all types of events, and thus, the power to detect effects, especially interactions, may have been very low (see also below).

#### *The Influence of Anxiety on the Likelihood of MDEs Depends on History of Depression*

The presence of co-occurring anxiety was associated with a higher likelihood of MDEs for those with a history of depression whereas it was not associated with the presence of MDEs for those without a history of depression. In other words, co-occurring anxiety was associated with a higher likelihood of recurrences, but it was not associated with a higher likelihood of first onsets. Similarly, the presence of pre-existing anxiety was associated with a higher likelihood of MDEs for those with a history of depression whereas it was associated with a lower likelihood of MDEs for those without a history of depression. That is, pre-existing anxiety was associated with a higher likelihood of recurrences, but a lower likelihood of first onsets.

These findings are not consistent with research indicating that current and lifetime history of AD predicts recurrences of depression (Giles et al., 1989; O'Leary et al., 2000), nor research suggesting that GAD predicts subsequent first onsets of MDE (Kessler et al.,



2008). Further, these findings are not consonant with the tendency for anxiety disorders to precede the development of depression (e.g., Kessler et al., 1996; Fava et al., 2000; cf. Moffit et al. 2007). Thus, these findings are difficult to interpret given their lack of correspondence with epidemiological data.

*No evidence that Pre-existing or Co-occurring Anxiety Influences the Occurrence of Life Events*

Contrary to my predictions, I did not find evidence that pre-existing or co-occurring anxiety influences the occurrence of life events: events were equally likely to be present prior to MDEs regardless of the presence of anxiety. This is inconsistent with research suggesting that those with comorbid anxiety experience higher rates of life events. For example, in one investigation, the median number of life events experienced (independent and dependent) in the one year prior to onset was significantly greater in comorbid (defined as co-occurring anxiety) as compared to non-comorbid participants (Leskela et al., 2004). It is also inconsistent with research on the impact of comorbid anxiety on stress generation (Hammen, 1991), as research suggests that individuals with comorbid anxiety (as well as other disorders) experience higher levels of dependent stress (Daley et al., 1997) and higher rates of dependent life events prior to episode onset (Harkness and Luther, 2001). Of note, these studies investigated the total life stress or frequency of life events, not the presence or absence of life events. In addition, Daley et al. investigated total life stress over a one year period, not necessarily proximal to onsets of depression. Thus, although the results suggest that anxiety will influence the occurrence of life events, especially dependent events, the studies do not directly measure

occurrence. Unfortunately, there is not other work to which to compare the present findings.

It is important to note that the power to detect interactions in the occurrence analyses was substantially lower than the power in the impact analyses by virtue of the number of lines per participant. In the occurrence analyses, each line represented an MDE. That meant that there were only multiple lines for participants if they experienced more than one MDE. If participants did not experience an MDE, then they only had one line of data for a random period. So, in the occurrence analyses, there were 205 lines of data, as compared to 783 lines in the impact analyses. As such, it may be the case that there were not significant findings in the occurrence analyses, because power to detect effects was low. Thus, rather than discouraging future research on the influence of anxiety on the occurrence of life events, there is a need for future research with a larger sample of participants and higher rates of comorbidity to adequately test the influence of anxiety on occurrence.

### *Summary*

Overall, I did not find evidence that anxiety presensitizes or prekindles individuals to depression prior to first onsets. However, I did find some evidence that anxiety influences the impact of certain life events, but these changes were not coupled with changes in the occurrence of life events.

As mentioned, these findings should be viewed as tentative at best, as they are based on a very small number of people with anxiety. As a result, there was very low power to detect effects and some of the interactions were not able to be tested. Therefore, replication is needed.

However, most conservatively, there is some evidence that anxiety influences the stress-depression association, and that its influence may be different for different types of life events. Promising directions of future research include investigating the differential effects of specific anxiety disorders and the potential that sensitization and/or kindling effects are specific to events which are directly related to the anxiety disorder(s) present. By examining more specific questions, it is possible not only to gain greater refinement of our knowledge of the role of anxiety in the stress-depression association, but potentially, more consistent effects will be evidenced with greater refinement of research questions.

### Summary

In addition to the limitations already discussed, several merit additional elaboration. One issue to consider is the generalizability of these results. In a recent meta-analysis of studies examining Post's model, support for the model varied according to age and gender, with less support evidenced in younger samples and females, as well as less support for community samples (Stroud et al., 2008). Given this sample is composed of young women recruited from the community, it is important to consider how these factors influenced the current results. But, as a summary of research in the field, the meta-analysis does not speak to changes in impact and occurrence of life events, as we investigated in the current study. As such, we can only conclude from the meta-analysis that the association may vary according to age, gender and patient status. Clearly, research examining both genders and individuals of different ages is needed, given that the current findings are based on a community sample of young women. In addition, recent work suggests that the relative importance of dependent events may increase with

age, as evidence for sensitization to LLEs as a function of childhood adversity was specific to independent events in a sample of adolescents (Harkness, Bruce & Lumley, 2006). The authors asserted that independent events may be more relevant to adolescents than dependent events, because adolescents may experience events caused by parents (e.g., moves, parent divorce), and therefore are less likely to experience dependent events. Given our sample was followed for five years, beginning at high school graduation (transition from adolescence to adulthood), it is unclear if age affected the specificity of changes in impact to independent events in the cross-sectional analyses. However, it seems unlikely because many participants experienced severe (e.g., abortions and romantic break-ups) and nonsevere dependent LLEs (e.g., moving out of the home for first time and failing a test). Still, this remains a possibility. In addition, it has been suggested that individuals may be particularly vulnerable to sensitization to stress during periods of developmental transition, such as puberty (Rudolph & Flynn, 2007). Our sample was followed during the transition to adulthood and in fact, some of the life events experienced were directly related to this transition, including moving out of the family home for the first time, leaving friends and family, and beginning college/work. As such, it will be important to investigate changes in the impact and occurrence of events at other more stable points in the life course. However, this may be challenging given that most individuals experience their first episode of depression in adolescence (Rudolph, 2008).

Another issue to consider is the potential that participants were receiving pharmacological treatment for their depression and/or anxiety. The exact number of participants who were treated with medication is unknown, but given the nature of the

sample, it is unlikely the rate of antidepressants was high. Post & Weiss (1998) have underscored the notion that sensitization and kindling processes are evident in untreated affective disorders. The authors noted that effective interventions, particularly medication, may be sufficient to reduce these processes. In addition, Monroe and colleagues (2006, 2007) have demonstrated differential effects of SLEs and LLEs on recurrences for medicated as compared to non-medicated patients. Thus, future investigations with community samples should carefully record medications and psychosocial interventions received by participants.

Finally, this investigation was limited to the presence or absence of episodic severe and non-severe events. Research has demonstrated that the association between chronic stress and depression also varies as a function of depression history (Daley et al., 1997) and some have suggested that chronic stress and episodic stress interact in predicting episodes of depression (Brown & Harris, 1989; Monroe et al., 2007). Thus, it is unclear if and to what extent chronic stress influenced the current findings. Further, although I focused on the presence or absence of events, other work has demonstrated that the cumulative impact of non-severe events also exhibits a pattern consistent with stress sensitization (Lenze et al., 2008). It follows that events may interact with each other such that, for example, the presence of one independent SLE in close proximity to 3 independent LLEs may have a different impact than one independent SLE occurring alone. Future work should consider interactions of episodic events and chronic stress, as well as minor daily stressors, in affecting the impact of life events.

Although I limited the current investigation to the influence of comorbid anxiety disorders, future work should examine the influence of other types of comorbidities. One

promising area of research is the influence of comorbid personality disorders, as other work on the stress-depression association has suggested that personality disorders (Daley, Hammen, Davila & Burge, 1998) and personality traits (e.g., neuroticism; Ormel et al., 2001) affect the association. By examining the influence of different comorbid disorders, we can develop a more comprehensive model of the association.

Overall, the results found in the current study are bolstered by the use of diagnostic interviews to assess depression, the focus on diagnosable depression and anxiety, the use of contextual interviews to assess episodic stress, and the precise dating of events and episodes. This study aimed to increase clarity about the nature of changes in the stress-depression association in first onsets versus recurrences. As such, I tested the SS and SA models by examining how the role of stress changes for both severe and nonsevere life events, using both cross-sectional and longitudinal analyses. With some exceptions, this work evidenced support for the SS model over the SA model, underscoring the notion that certain types of stress, particularly uncontrollable losses in close interpersonal relationships, increase in their importance with successive episodes. I also examined the influence of a lifetime history and concurrent anxiety disorder(s) on the stress-depression association. Although limited in power, there was some evidence that anxiety influences the impact of life events. Most importantly for clinical interventions, there is some evidence that a history of anxiety renders dependent SLEs more potent with successive episodes.

This has several clinical implications. Because the impact of independent events was greater in those with a history of depression and the impact of dependent severe events amplified with successive episodes in those with pre-existing anxiety, it is

important to develop coping strategies to decrease the subjective impact of events when working with individuals with a history of depression and/or a lifetime history of anxiety. Research indicates that a lack of control over stressors increases stress responses and leads to depressive reactions (e.g., Abramson, Seligman, & Teasdale, 1978). It follows that if interventions increase individuals' perceived control over their environment, the chance of recurrence will decrease. Second, the cross-sectional findings highlighting the role of loss underscore the importance of interpersonally oriented therapies for depression. For example, interpersonal psychotherapy for depression specifically focuses on the role of loss events in the etiology of depression and works with individuals to process and overcome events of loss (Weissman, Markowitz, & Klerman, 2000). Third, the findings point to the importance of early losses and early uncontrollable events as well as anxiety as risk factors for depression. As discussed, Bowlby (1980) highlighted the key role of loss in setting the stage for depression, and we know from research on childhood adversity, that loss events and separations are more likely to trigger depression in individuals with a history of childhood adversity (Harkness et al., 2006). Similarly, others have highlighted the role of uncontrollable events in leading to the development of anxiety via a tendency to perceive future events as uncontrollable (e.g., Chorpita & Barlow, 1998). Thus, children and adolescents with early losses and uncontrollable negative events are a key group to target in the prevention of anxiety and depression.

In conclusion, these findings highlight the complexity of the relationships between stress, depression and anxiety as well as underscore several avenues for future investigations. Those avenues that will be most fruitful will continue to move beyond the general notion that the stress-depression association changes with successive recurrences.

## FOOTNOTES

<sup>1</sup>In a few cases, it was not clear whether or not events preceded episodes (herein called “questionable events”). To be conservative, the analyses presented in the text do not include the questionable events. However, all analyses were run with and without the questionable events, and including the questionable events did not change the results.

<sup>2</sup>Unfortunately, because these studies did not examine the impact and occurrence of life events, the language cannot be refined passed “salient”.

<sup>3</sup>However, if biological stress mechanisms, such as HPA axis functioning, were altered by the presence of anxiety, then analyses should have evidenced enhanced impact for all types of events.



Table 1

*Model predictions for the changes in impact and occurrence of SLEs and LLEs with successive recurrences*

SS Model	SA model
Impact	
•The impact of SLEs increases.	•The impact of SLEs decreases.
•The impact of LLEs increases.	•The impact of LLEs decreases.
Occurrence	
•The occurrence of precipitating SLEs decreases.	•The occurrence of precipitating SLEs decreases.
•The occurrence of precipitating LLEs increases.	•The occurrence of precipitating LLEs decreases.

Table 2

*Predictions of the SS and SA models*

SS Model	SA Model
SLEs	
<p>The impact of SLEs increases with repeated episodes, such that the probability of MDE, given the presence of an SLE, is greater for recurrences than first onsets.</p> $P(\text{MDE} \text{SLE}, \text{DHX}+) > P(\text{MDE} \text{SLE}, \text{DHX}-)$	<p>The impact of SLEs decreases with repeated episodes, such that the probability of MDE, given the presence of an SLE, is greater for first onsets than recurrences.</p> $P(\text{MDE} \text{SLE}, \text{DHX}+) < P(\text{MDE} \text{SLE}, \text{DHX}-)$
<p>The occurrence of SLEs decreases with repeated episodes, such that the probability of a precipitating SLE, given an MDE, is greater for first onsets than recurrences.</p> $P(\text{SLE} \text{MDE}, \text{DHX}+) < P(\text{SLE} \text{MDE}, \text{DHX}-)$	<p>The occurrence of SLEs decreases with repeated episodes, such that the probability of a precipitating SLE, given an MDE, is greater for first onsets than recurrences.</p> $P(\text{SLE} \text{MDE}, \text{DHX}+) < P(\text{SLE} \text{MDE}, \text{DHX}-)$
LLEs	
<p>The impact of LLEs increases with repeated episodes, such that the probability of MDE, given the presence of an LLE, is greater for recurrences than first onsets.</p> $P(\text{MDE} \text{LLE}, \text{DHX}+) < P(\text{MDE} \text{LLE}, \text{DHX}-)$	<p>The impact of LLEs decreases with repeated episodes, such that the probability of MDE, given the presence of an LLE, is greater for first onsets than recurrences.</p> $P(\text{MDE} \text{LLE}, \text{DHX}+) < P(\text{MDE} \text{LLE}, \text{DHX}-)$
<p>The occurrence of LLEs increases with repeated episodes, such that the probability of a precipitating LLE, given an MDE, is greater for recurrences than first onsets.</p> $P(\text{LLE} \text{MDE}, \text{DHX}+) > P(\text{LLE} \text{MDE}, \text{DHX}-)$	<p>The occurrence of LLEs decreases with repeated episodes, such that the probability of a precipitating LLE, given an MDE, is greater for first onsets than recurrences.</p> $P(\text{LLE} \text{MDE}, \text{DHX}+) < P(\text{LLE} \text{MDE}, \text{DHX}-)$

Table 3

*Calculations for computing the conditional probabilities for the impact of life events*

First Onsets	Recurrences
Dependent SLEs (worst)	
$P(\text{MDE} \text{SLE}) = P(\text{MDE} + \text{SLE}) / P(\text{SLE})$ $= (5/61) / (5/61)$ $= 1.00^*$	$P(\text{MDE} \text{SLE}) = P(\text{MDE} + \text{SLE}) / P(\text{SLE})$ $= (4/88) / (6/88)$ $= .67^*$
Independent SLEs (worst)	
$P(\text{MDE} \text{SLE}) = P(\text{MDE} + \text{SLE}) / P(\text{SLE})$ $= (7/60) / (7/60)$ $= 1.00^*$	$P(\text{MDE} \text{SLE}) = P(\text{MDE} + \text{SLE}) / P(\text{SLE})$ $= (12/89) / (15/89)$ $= .80^*$
Dependent SLEs (random)	
$P(\text{MDE} \text{SLE}) = P(\text{MDE} + \text{SLE}) / P(\text{SLE})$ $= (5/86) / (54/86)$ $= .09$	$P(\text{MDE} \text{SLE}) = P(\text{MDE} + \text{SLE}) / P(\text{SLE})$ $= (8/64) / (49/64)$ $= .16$
Independent SLEs (random)	
$P(\text{MDE} \text{SLE}) = P(\text{MDE} + \text{SLE}) / P(\text{LLE})$ $= (4/88) / (59/88)$ $= .07^*$	$P(\text{MDE} \text{SLE}) = P(\text{MDE} + \text{SLE}) / P(\text{LLE})$ $= (15/61) / (46/61)$ $= .33^*$
Dependent LLEs (random)	
$P(\text{MDE} \text{LLE}) = P(\text{MDE} + \text{LLE}) / P(\text{LLE})$ $= (4/85) / (85/85)$ $= .05$	$P(\text{MDE} \text{LLE}) = P(\text{MDE} + \text{LLE}) / P(\text{LLE})$ $= (5/64) / (64/64)$ $= .08$
Independent LLEs (random)	
$P(\text{MDE} \text{LLE}) = P(\text{MDE} + \text{LLE}) / P(\text{LLE})$ $= (2/84) / (73/84)$ $= .03^*$	$P(\text{MDE} \text{LLE}) = P(\text{MDE} + \text{LLE}) / P(\text{LLE})$ $= (11/65) / (64/65)$ $= .17^*$

\* $p < .05$

*Notes.* SLE = severe life event; LLE = lower level life event; MDE = Major Depressive Episode; P = probability.

Table 4

*Calculations for computing the conditional probabilities for the occurrence of life events*

First Onsets	Recurrences
Dependent SLEs	
$P(SLE MDE) = P(MDE + SLE) / P(MDE)$ $= (13/103) / (37/103)$ $= .35^*$	$P(SLE MDE) = P(MDE + SLE) / P(MDE)$ $= (5/47) / (34/47)$ $= .14^*$
Independent SLEs	
$P(SLE MDE) = P(MDE + SLE) / P(MDE)$ $= (10/103) / (37/103)$ $= .27$	$P(SLE MDE) = P(MDE + SLE) / P(MDE)$ $= (10/47) / (34/47)$ $= .29$
Dependent LLEs	
$P(LLE MDE) = P(MDE + LLE) / P(MDE)$ $= (26/103) / (37/103)$ $= .70$	$P(LLE MDE) = P(MDE + LLE) / P(MDE)$ $= (18/47) / (34/47)$ $= .53$
Independent LLEs	
$P(LLE MDE) = P(MDE + LLE) / P(MDE)$ $= (10/103) / (37/103)$ $= .27$	$P(LLE MDE) = P(MDE + LLE) / P(MDE)$ $= (10/47) / (34/47)$ $= .29$

\* $p < .05$

*Notes.* SLE = severe life event; LLE = lower level life event; MDE = Major Depressive Episode; P = probability.

Table 5

*Frequency of life events in the longitudinal with-in person analyses*

Impact		
Event	No History of Depression	History of Depression
Independent SLE	107 (24.3)	93 (27.1)
Independent LLE	216 (49.8)	200 (57.3)
Dependent SLE	91 (20.8)	98 (28.3)
Dependent LLE	395 (90.8)	302 (86.8)
Occurrence		
Event	First Onsets	Recurrences
Independent SLE	16 (15.5)	23 (22.3)
Independent LLE	37 (35.9)	21 (20.4)
Dependent SLE	16 (15.5)	16 (15.5)
Dependent LLE	64 (62.1)	62 (60.2)

*Notes.* Percentages are in parentheses. Frequencies and parentheses are based on the total number of lines in the datasets. For impact, the frequency is the number of life events in the data set, independent of episodes of depression. For occurrence, the frequency is the number of individuals who experienced the event prior to a first onset or recurrence of depression. SLE = severe life event; LLE = lower level life event.

Table 6

*Longitudinal within-person analyses examining the impact of life events*

Model	Effect	Estimate	<i>t</i>
SLE independent	Event	.036	1.08
	History of MDE	.095	3.53**
	Interaction (Event X History of MDE)	.055	1.12
LLE independent	Event	-.006	-.201
	History of MDE	.156	4.88**
	Interaction (Event X History of MDE)	-.025	-.61
SLE dependent	Event	.040	1.27
	History of MDE	.076	3.17**
	Interaction (Event X History of MDE)	-.027	.15
LLE dependent	Event	-.126	-2.55*
	History of MDE	.228	3.46**
	Interaction (Event X History of MDE)	-.176	-2.57*

*Notes.*  $n = 149$ ; SLE = severe life event; LLE = lower level life event; MDE = Major Depressive Episode.

\* $p = .01$ ; \*\*  $p < .01$

Table 7

*Longitudinal within-person analyses examining the occurrence of life events*

Model	Effect	Estimate	<i>t</i>
SLE independent	MDE	.183	2.43*
	History of MDE	-.091	-.84
	Interaction (MDE X History of MDE)	.080	.61
LLE independent	MDE	.026	.30
	History of MDE	.017	.14
	Interaction (MDE X History of MDE)	.129	.85
SLE dependent	MDE	.307	4.44**
	History of MDE	.097	.98
	Interaction (MDE X History of MDE)	-.324	-2.73**
LLE dependent	MDE	.111	1.10
	History of MDE	.154	1.06
	Interaction (MDE X History of MDE)	-.214	-1.24

*Notes.*  $n = 149$ ; SLE = severe life event; LLE = lower level life event; MDE = Major Depressive Episode.

\*\*  $p < .01$



Table 8

*Frequency of lifetime AD and concurrent AD in the cross-sectional analyses examining the influence of anxiety on the impact and occurrence of life events*

	Lifetime AD	Concurrent AD
Event		Impact
Worst SLE independent	15 (14.4)	1 (1)
Random SLE independent	15 (13.5)	2 (1.8)
Random LLE independent	21 (15.3)	6 (4.4)
Worst SLE dependent	13 (12.6)	5 (4.9)
Random SLE dependent	12 (11.5)	2 (1.9)
Random LLE dependent	20 (13.4)	1 (0.7)
		Occurrence
MDE	18 (25.7)	8 (11.4)

*Notes.* SLE = severe life event; LLE = lower level life event; AD = Anxiety Disorder; MDE = Major Depressive Episode. Percentages are in parentheses. Frequencies and percentages are based on the total number of participants. For impact, lifetime AD is defined as the presence of anxiety prior to the event and concurrent AD is defined as the presence of anxiety at the same time as the event. For occurrence, lifetime AD is defined as the presence of anxiety prior to the MDE and concurrent AD is defined as the presence of anxiety at the same time as the MDE.

Table 9

*Cross-sectional analyses examining the influence of lifetime anxiety on the impact of life events*

Event logistic regression model	Entry Step	Variable	Wald	B	S.E.	p
Worst SLE independent	1	Presence of MDE	5.15	1.33	.59	.02
	2	Presence of Lifetime AD	8.71	2.43	.82	.00
	3	Interaction (MDE x AD)	1.31	-1.74	.25	.18
Random SLE independent	1	Presence of MDE	7.43	1.74	.64	.00
	2	Presence of Lifetime AD	7.16	2.21	.83	.00
	3	Interaction (MDE x AD)	.00	18.08	17970	.99
Random LLE independent	1	Presence of MDE	5.19	2.48	1.09	.02
	2	Presence of Lifetime AD	8.87	2.00	.67	.00
	3	Interaction (MDE x AD)	2.30	-2.56	1.69	.13
Worst SLE dependent	1	Presence of MDE	.78	.70	.80	.38
	2	Presence of Lifetime AD	.00	21.62	12120	.99

	3	Interaction (MDE x AD)	.00	-43.11	30900	.99
Random SLE	1	Presence of MDE	2.93	1.24	.73	.09
dependent	2	Presence of Lifetime AD	.00	21.60	12710	.99
	3	Interaction (MDE x AD)	.00	-43.65	31130	.99
Random LLE	1	Presence of MDE	.17	.32	.79	.68
dependent	2	Presence of Lifetime AD	12.07	2.69	.77	.00
	3	Interaction (MDE x AD)	.00	18.80	28420	.99

*Notes.* *ns* = 103-149; SLE = severe life event; LLE = lower level life event; MDE = Major Depressive Episode; AD = Anxiety Disorder; Wald = Wald Chi-Square Statistic; *B* = estimated multinomial logistic regression coefficient; S.E. = Standard Error.

Table 10

*Cross-sectional analyses examining the influence of concurrent anxiety on the impact of life events*

Event logistic regression model	Entry Step	Variable	Wald	<i>B</i>	<i>S.E.</i>	<i>p</i>
Worst SLE independent	1	Presence of MDE	4.99	1.18	.53	.03
	2	Presence of Concurrent AD	.00	21.84	40190	1.00
	3	Interaction (MDE x AD)	-	-	-	-
Random SLE independent	1	Presence of MDE	9.41	1.87	.61	.00
	2	Presence of Concurrent AD	.00	21.82	40190	1.00
	3	Interaction (MDE x AD)	.00	-1.87	56840	1.00
Random LLE independent	1	Presence of MDE	6.09	1.97	.80	.01
	2	Presence of Concurrent AD	2.37	1.74	1.13	.12
	3	Interaction (MDE x AD)	.00	17.85	40190	1.00

Worst SLE dependent	1	Presence of MDE	.09	.22	.74	.76
	2	Presence of Concurrent AD	.00	21.43	20100	.99
	3	Interaction (MDE x AD)	.00	-42.63	44940	.99
Random SLE dependent	1	Presence of MDE	1.17	.71	.66	.28
	2	Presence of Concurrent AD	.00	21.36	41090	1.00
	3	Interaction (MDE x AD)	.00	-43.12	56840	.99
Random LLE dependent	1	Presence of MDE	.65	.56	.70	.42
	2	Presence of Concurrent AD	.00	21.54	40190	1.00
	3	Interaction (MDE x AD)	-	-	-	-

*Notes.* ns = 103-149; SLE = severe life event; LLE = lower level life event; MDE = Major Depressive Episode; AD = Anxiety Disorder; Wald = Wald Chi-Square Statistic; *B* = estimated multinomial logistic regression coefficient; S.E. = Standard Error.

Table 11

*Cross-sectional analyses examining the influence of lifetime anxiety on the occurrence of life events*

Event logistic regression model	Entry Step	Variable	Wald	B	S.E.	p
SLE independent	1	Presence of event	.24	.29	.59	.63
	2	Presence of Lifetime AD	1.05	.73	.71	.31
	3	Interaction (Event x AD)	.00	.07	1.20	.96
LLE independent	1	Presence of event	.03	.11	.63	.87
	2	Presence of Lifetime AD	.50	.51	.72	.48
	3	Interaction (Event x AD)	.23	.59	1.21	.63
SLE dependent	1	Presence of event	1.32	-.79	.69	.25
	2	Presence of Lifetime AD	3.25	1.51	.84	.07
	3	Interaction (Event x AD)	1.25	-1.51	1.35	.26
LLE dependent	1	Presence of event	.03	.11	.63	.87
	2	Presence of Lifetime AD	.50	.51	.72	.48

3	Interaction (Event x AD)	.23	.59	1.21	.63
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*Notes.*  $n = 70$ ; SLE = severe life event; LLE = lower level life event; MDE = Major Depressive Episode; AD = Anxiety Disorder; Wald = Wald Chi-Square Statistic;  $B$  = estimated multinomial logistic regression coefficient; S.E. = Standard Error.

Table 12

*Cross-sectional analyses examining the influence of concurrent anxiety on the occurrence of life events*

Event logistic regression model	Entry Step	Variable	Wald	<i>B</i>	<i>S.E.</i>	<i>p</i>
SLE independent	1	Presence of event	.83	.50	.55	.36
	2	Presence of Concurrent AD	1.00	1.19	1.20	.32
	3	Interaction (Event x AD)	.97	-1.60	1.62	.33
LLE independent	1	Presence of event	.02	.07	.57	.90
	2	Presence of Concurrent AD	.34	-.74	1.26	.56
	3	Interaction (Event x AD)	1.31	2.00	1.76	.25
SLE dependent	1	Presence of event	2.43	-.92	.59	.12
	2	Presence of Concurrent AD	.46	.60	.90	.50
	3	Interaction (Event x AD)	.00	-21.99	40190	1.00
LLE dependent	1	Presence of event	.02	.07	.57	.90
	2	Presence of	.34	-.74	1.26	.56



		Concurrent AD			
3	Interaction (Event x AD)	1.31	2.00	1.75	.25

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*Notes.*  $n = 70$ ; SLE = severe life event; LLE = lower level life event; MDE = Major Depressive Episode; AD = Anxiety Disorder; Wald = Wald Chi-Square Statistic;  $B$  = estimated multinomial logistic regression coefficient; S.E. = Standard Error.

Table 13

*Longitudinal within-person analyses examining the influence of anxiety on the impact of life events*

Model	Effect	Lifetime AD		Concurrent AD	
		Estimate	<i>t</i>	Estimate	<i>t</i>
SLE	Event	.038	1.13	.033	1.02
independent	History of MDE	.087	3.02***	.089	3.36***
	AD	.045	.49	-.041	-.30
	Interaction (Event x History of MDE)	.043	.82	.059	1.20
	Interaction (AD x History of MDE)	.046	.66	.518	3.17***
	Interaction (Event x AD)	-.103	-.49	-.679	-3.97***
	Interaction (AD x Event x History of MDE)	.040	.18	0	-
	LLE	Event	-.007	-.25	-.007
independent	History of MDE	.138	3.98***	.138	4.33***
	AD	-.049	-.45	-.051	-.31
	Interaction (Event x History of MDE)	-.020	-.44	-.012	-.28
	Interaction (AD x History of MDE)	.138	1.11	.584	2.96***

	History of MDE)				
	Interaction (Event x	.020	.13	.028	.11
	AD)				
	Interaction (AD x	-.044	-.25	-.296	-.99
	Event x History of				
	MDE)				
SLE	Event	.031	.99	.034	1.10
dependent	History of MDE	.071	2.70***	.067	2.75***
	AD	-.034	-.41	-.036	-.30
	Interaction (Event x	-.047	-1.01	-.062	-1.42
	History of MDE)				
	Interaction (AD x	.102	1.01	.648	4.36***
	History of MDE)				
	Interaction (Event x	1.01	3.07***	-.671	-4.60***
	AD)				
	Interaction (AD x	-1.16	-3.48***	0	-
	Event x History of				
	MDE)				
LLE	Event	-.132	-2.65***	-.131	-2.69***
dependent	History of MDE	.134	1.92 <sup>a</sup>	.134	2.04**
	AD	-.181	-.86	-.174	-.60
	Interaction (Event x	-.092	-1.26	-.085	-1.24
	History of MDE)				

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Interaction (AD x History of MDE)	.457	1.97*	.828	2.63**
Interaction (Event x AD)	.113	.50	.121	.38
Interaction (AD x Event x History of MDE)	-.373	-1.51	-.731	-2.07**

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*Notes.*  $n = 149$ ; SLE = severe life event; LLE = lower level life event; MDE = Major Depressive Episode; AD = Anxiety Disorder.  
 \*  $p = .05$ ; \*\*  $p < .05$ ; \*\*\*  $p < .01$ ; <sup>a</sup>  $p = .06$

Table 14

*Longitudinal within-person analyses examining the influence of anxiety on the occurrence of life events*

Model	Effect	Lifetime AD		Concurrent AD	
		Estimate	<i>t</i>	Estimate	<i>t</i>
SLE	MDE	.175	2.169**	.152	1.98*
independent	History of MDE	-.092	-.79	-.091	-.84
	AD	-.092	-.25	.389	1.77
	Interaction (MDE x History of MDE)	.087	.61	.109	.826
	Interaction (AD x History of MDE)	.092	.20	-.277	-1.07
	Interaction (MDE x AD)	.135	.33	0	-
	Interaction (AD x MDE x History of MDE)	-.111	-.22	0	-
LLE	MDE	.001	.01	.017	.19
independent	History of MDE	-.033	.80	.017	.14
	AD	-.200	-.47	.110	.67
	Interaction (MDE x History of MDE)	.202	1.22	.118	.44
	Interaction (AD x History of MDE)	.533	.99	.166	.58
	Interaction (MDE x AD)	.337	.72	0	-

	Interaction (AD x MDE x History of MDE)	-.659	-1.13	0	-
SLE dependent	MDE	.244	3.37***	.310	4.36** *
	History of MDE	.120	1.51	.097	.980
	AD	-.046	-.14	-.023	-.12
	Interaction (MDE x History of MDE)	-.277	-2.15**	-.290	- 2.39**
	Interaction (AD x History of MDE)	-.121	-.29	-.139	-.67
	Interaction (MDE x AD)	.435	1.19	0	-
	Interaction (AD x MDE x History of MDE)	-.255	-.563	0	-
LLE dependent	MDE	.138	1.29	.115	1.10
	History of MDE	.097	.63	.154	1.05
	AD	-.570	-1.15	-.024	-.08
	Interaction (MDE x History of MDE)	-.197	-1.05	-.192	-1.09
	Interaction (AD x History of MDE)	.903	1.45	-.188	-.55
	Interaction (MDE x AD)	.347	.64	0	-
	Interaction (AD x MDE x History of MDE)	-.681	-1.02	0	-

*Notes.*  $n = 149$ ; SLE = severe life event; LLE = lower level life event; MDE = Major Depressive Episode; AD = Anxiety Disorder.

\*  $p = .05$ ; \*\*  $p < .05$ ; \*\*\*  $p < .01$

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