

Dynamic Associations Between Stressful Life Events and Adolescent Internalizing Psychopathology in a Multiwave Longitudinal Study

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Associations between stressful life events (SLEs) and internalizing psychopathology are complex and bidirectional, involving interactions among stressors across development to predict psychopathology (i.e., stress sensitization) and psychopathology predicting greater exposure to SLEs (i.e., stress generation). Although stress sensitization and generation theoretical models inherently focus on within-person effects, most previous research has compared average levels of stress and psychopathology across individuals in a sample (i.e., between-person effects). The present study addressed this gap by investigating stress sensitization and stress generation effects in a multiwave, prospective study of SLEs and adolescent depression and anxiety symptoms. Depression, anxiety, and SLE exposure were assessed every 3 months for 2 years (8 waves of data) in a sample of adolescents ($n = 382$, aged 11 to 15 at baseline). Multilevel modeling revealed within-person stress sensitization effects such that the association between within-person increases in SLEs and depression, but not anxiety, symptoms were stronger among adolescents who experienced higher average levels of SLEs across 2 years. We also observed within-person stress generation effects, such that adolescents reported a greater number of dependent-interpersonal SLEs during time periods after experiencing higher levels of depression at the previous wave than was typical for them. Although no within-person stress generation effects emerged for anxiety, higher overall levels of anxiety predicted greater exposure to dependent-interpersonal SLEs. Our findings extend prior work by demonstrating stress sensitization in predicting depression following normative forms of SLEs and stress generation effects for both depression and anxiety using a multilevel modeling approach. Clinical implications include an individualized approach to interventions.

General Scientific Summary

This study demonstrates that adolescents who report more overall stress compared to others experience greater depression symptoms during months when their own stress level is higher than is typical for them. We also show that adolescents report greater exposure to interpersonal stressors that are partly dependent upon an individual's characteristics or behaviors after months when they experience higher depression symptoms than is typical for them, whereas higher overall symptoms of anxiety predicted greater exposure to such stressors. This research suggests a two-way relationship between stress and symptoms of depression and anxiety and may help mental health professionals better understand how stress, depression, and anxiety are related within a particular individual.

Keywords: stress sensitization, stress generation, depression, anxiety, adolescents

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Exposure to stressful life events (SLEs) is a robust predictor of internalizing psychopathology, including depression (Hammen, 2005; Harkness, Bruce, & Lumley, 2006) and anxiety (Espejo et al., 2007; McLaughlin et al., 2012). Adolescence involves not only higher levels of exposure to SLEs (Larson & Lampman-Petratis, 1989), but these experiences are more tightly coupled with increases in negative affect (Larson & Ham, 1993) and psychopathology (Monroe, Rohde, Seeley, & Lewinsohn, 1999) than in other developmental periods. The associations between SLEs and internalizing psychopathology are complex, with bidirectional influences and cascading effects over time (e.g., Hankin & Abramson, 2001). Stress generation is well documented in adolescents, such that the presence of internalizing psychopathology is associated with greater likelihood of experiencing SLEs that are generated, at least in part, by the adolescent (Hammen, 1991, 2005; Rudolph, 2008). Stress sensitization effects have also been observed during this period, such that exposure to stressors earlier in development heightens vulnerability for depression and anxiety following later stressors (Espejo et al., 2007; Hammen, Henry, & Daley, 2000). However, the vast majority of previous research on stress sensitization and generalization related to internalizing psychopathology in adolescents has relied on between-person approaches that compare average levels of stress across individuals in a sample. Between-person approaches are at odds with theoretical models of stress and psychopathology, which focus on *within-person* effects, such as how stress and psychopathology are related within a given individual (Curran & Bauer, 2011). In other words, these approaches confound individual differences in *who* is exposed to stress with the predictors and outcomes of occasions *when* individuals are exposed. The present study addressed this limitation by using a multiwave, prospective design to investigate the dynamic interplay between SLEs and internalizing psychopathology over time during adolescence.

The stress sensitization hypothesis proposes that exposure to adversity early in development heightens vulnerability for developing depression and anxiety following subsequent stressors (Hammen, 2005; Hammen et al., 2000). Exposure to adversity early in development is associated with heightened emotional reactivity at neural (Hein & Monk, 2017; McLaughlin, Peverill, Gold, Alves, & Sheridan, 2015), psychophysiological (Lambert, King, Monahan, & McLaughlin, 2017; Starr et al., 2017), and behavioral measures (Heleniak, Jenness, Vander Stoep, McCauley, & McLaughlin, 2016; Lambert et al., 2017). A wide range of emotion regulation difficulties, ranging from attentional deployment to emotional stimuli (Pollak & Tolley-Schell, 2003) to engagement in high levels of maladaptive regulation strategies like rumination (Heleniak et al., 2016), have also been observed among those who have experienced early life adversity. These alterations in emotional reactivity and regulation following chronic exposure to stress have been posited as a mechanism underlying stress sensitization effects by increasing the intensity and duration of emotional responses to subsequent SLEs. In a seminal study, Hammen and colleagues (2000) demonstrated that lower levels of exposure to SLEs were more strongly associated with depression among females with a history of childhood adversity than those who had never encountered adversity. Subsequent studies have demonstrated a similar pattern, whereby adolescents and adults with a history of exposure to childhood adversity were more likely to develop depression and anxiety after experiencing SLEs (Espejo et al., 2007; Harkness et

al., 2006; McLaughlin, Conron, Koenen, & Gilman, 2010; Rudolph & Flynn, 2007; Starr, Hammen, Conway, Raposa, & Brennan, 2014). Notably, although some of these studies have used a longitudinal design to examine the stress sensitization hypothesis (Espejo et al., 2007; Hammen et al., 2000; Rudolph & Flynn, 2007; Starr et al., 2014), all focused on between-person effects.

Several studies have used intense repeated-measures designs such as daily diaries or experience sampling methodology to examine the stress sensitization hypothesis in a within-person framework, demonstrating that adults with a history of child maltreatment exhibit greater negative affect in response to daily stress compared to those without a history of childhood adversity (Glaser, van Os, Portegijs, & Myin-Germeys, 2006; Wichers et al., 2009). Although informative, these studies focused on daily stress and affect over the course of several days, which does not allow for examination of links between SLEs and symptoms of psychopathology over a time frame more relevant to symptom development and disorder onset (i.e., weeks to months; Hammen, 2005; Monroe & Reid, 2008). One recent study using a within-person statistical approach and multiwave design over 2.5 years demonstrated that adults with a history of emotional maltreatment developed greater depression symptoms following SLEs than those without a maltreatment history (Shapero et al., 2014). Studies utilizing multiwave, prospective designs to determine whether the stress sensitization processes increase vulnerability to internalizing psychopathology following recent exposure to SLEs in children and adolescents are notably lacking. Furthermore, existing work has largely examined stress sensitization within the context of exposure to childhood adversity, ranging from child maltreatment (Harkness et al., 2006; McLaughlin, Conron, et al., 2010) to experiences like parental divorce and marital discord (Espejo et al., 2007; Hammen et al., 2000). The role that recent experiences of developmentally normative SLEs (e.g., bullying, failing a test, peer conflict) play in sensitizing adolescents to depression and anxiety following subsequent SLEs has rarely been examined. We do so in the current report.

In addition to stress sensitization work demonstrating the interplay between SLEs occurring at different points in development and internalizing psychopathology, extensive evidence supports a bidirectional association between exposure to SLEs and internalizing symptoms. Hammen's (1991) seminal work on stress generation demonstrated that adult women with depression experienced more SLEs that are partly dependent upon an individual's characteristics or behaviors (i.e., dependent SLEs) over time compared to women without psychopathology. Subsequent studies have replicated these findings among children and adolescents with high levels of depression and anxiety, particularly in the generation of dependent-interpersonal SLEs (e.g., Hammen & Brennan, 2001; McLaughlin & Nolen-Hoeksema, 2012; Rudolph, 2008; Shapero, Hankin, & Barrocas, 2013; Shih, Abela, & Starrs, 2009). Likely mechanisms of this association including personality traits (Kendler, Gardner, & Prescott, 2003; Starrs et al., 2017), interpersonal difficulties (Bos, Bouhuys, Geerts, Van Os, & Ormel, 2006; Shih, Barstead, & Dianno, 2018), corumination (Hankin, Stone, & Wright, 2010), and attachment style (Hankin, Kassel, & Abela, 2005) have also been investigated. However, the majority of stress generation studies in developmental samples have been cross-sectional (Hammen & Brennan, 2001; Starrs et al., 2010), used two time-point designs (Shih et al., 2009), or relied on between-person

statistical approaches (Rudolph, Flynn, Abaied, Groot, & Thompson, 2009; Starr et al., 2017). These approaches are unable to capture how within-person associations between stress and internalizing symptoms unfold over time; in other words, they cannot test the hypothesis that when a particular adolescent experiences higher levels of depression or anxiety symptoms, they are more likely to subsequently experience SLEs. Only one study, to our knowledge, has used multilevel modeling to demonstrate that within-person fluctuations in depression symptoms predict fluctuations in SLEs across 5 months in a community sample of youth (Shapero et al., 2013).

Bidirectional theories of stress–psychopathology associations, including stress sensitization and stress generation, involve hypotheses about within-person processes (Abela & Hankin, 2008). For example, stress generation theories hypothesize that when youth experience symptoms of anxiety and depression the likelihood that they will generate more SLEs in their lives increases. However, as previously noted, the majority of studies have used between-person designs or statistical approaches in order to make inferences about these within-person processes, an error of inference referred to as the ecological fallacy (Blakely & Woodward, 2000; Curran & Bauer, 2011). Prior research has documented between-person differences in the propensity to experience SLEs (King, Molina, & Chassin, 2008). Between-person differences in SLEs likely reflect relatively stable individual differences, such as neuroticism or exposure to poverty, that raise exposure to SLEs (Kendler et al., 2003); however, between-person study designs can only provide information about such individual differences. For instance, a person may report high levels of exposure to SLEs and meet criteria for depression, whereas another may report no recent SLEs or depressive symptoms, and this does not imply that either person is likely to experience more SLEs when they become depressed. By aggregating information across multiple assessments, within-person models can directly test the assumption that when a person experiences more depression symptoms, they are more likely to develop SLEs relative to periods when they experienced an absence of symptoms. Although within-person designs have been used to test hypotheses about the relation between stress and alcohol use (King, Molina, & Chassin, 2009), cognitive vulnerability (Abela & Hankin, 2011), and genetic factors (Hankin, Jenness, Abela, & Smolen, 2011), these designs and related analytic techniques have rarely been used in the stress sensitization and generation literatures.

Further, although previous stress-sensitization research has examined childhood adversity as a moderating influence on symptom development, there has been less focus on how normative stressors may influence the likelihood of experiencing increases in internalizing symptoms following subsequent SLEs. Therefore, there is a need to not only examine between- and within-person effects, but the interaction between the two when testing the stress sensitization hypothesis. This approach has clinical relevance, especially for individualizing mental health care approaches. For example, it could be useful for a clinician to know whether a relative increase in SLEs would be more likely to lead to later symptom increases for a child who generally experiences high or low levels of stress. Indeed, in contrast to the stress sensitization pattern, other evidence suggests a diminishing impact of SLEs on the onset and persistence of psychopathology, such that the incremental effect of each additional SLE gets smaller as the number of exposures increases (Green et al., 2010; Kessler et al., 2010; McLaughlin,

Green, et al., 2010). As previous work within the stress sensitization literature has not examined the interaction of between- and within-person effects of stress on psychopathology, this alternative has not yet been explored.

Adolescence is a key developmental period in which to investigate bidirectional models of stress and internalizing psychopathology. Most individuals experience their first onset of depression and anxiety during adolescence (Costello, Egger, & Angold, 2004; Hankin et al., 1998), and adolescent-onset depression and anxiety has been shown to substantially increase the risk for recurrence of internalizing disorders in adulthood (Rutter, Kim-Cohen, & Maughan, 2006). Moreover, first onsets of depression and anxiety are more closely tied to the experience of SLEs than subsequent, recurrent episodes (Chou, Mackenzie, Liang, & Sareen, 2011; Lewinsohn, Allen, Seeley, & Gotlib, 1999). Indeed, as many as half of all depression onsets in adolescence occur in the immediate aftermath of a stressor (Grant, Compas, Thurm, McMahon, & Gipson, 2004; Monroe et al., 1999). Exposure to SLEs increases during the transition to adolescence, and stressors become more tightly coupled with increases in negative affect and changes in physiological reactivity (Gunnar, Wewerka, Frenn, Long, & Griggs, 2009; Larson & Ham, 1993; Stroud et al., 2009). Understanding the dynamic, bidirectional associations between SLEs and depression and anxiety symptoms across the transition to adolescence is of critical importance given the developmental changes in exposure and reactivity to SLEs that accompany the substantial increase in risk for depression and anxiety during this period.

The present study addressed several gaps in the stress sensitization and generation literatures in youth. We measured exposure to SLEs, depression, and anxiety symptoms every 3 months across 2 years in a large community-based sample of adolescents (aged 11–15 at baseline). We applied a novel test of the stress sensitization hypothesis by investigating whether vulnerability to anxiety and depression following SLEs was greater for adolescents who had higher or lower levels of exposure to SLEs on average across the 2-year study period (i.e., an interaction of between- and within-person effects). This approach allowed us to test both the stress sensitization hypothesis, positing that youths with higher average levels of exposure to SLEs will be at greater risk for symptom development on months when they experience an increase in SLEs compared to their own average, and the competing hypothesis that youth with higher average levels of stress exposure will be less likely to develop symptoms on months characterized by increases in SLEs relative to youths with lower average levels of stress. To examine the bidirectional association between internalizing symptoms and stress, we tested for stress generation effects positing that youths will be at greater risk for experiencing dependent-interpersonal SLEs on months when they experience an increase in depression or anxiety symptoms relative to their own average levels of symptoms.

Method

Participants

Participants were recruited in Montreal, Quebec, Canada and Chicago, Illinois through advertisements in local newspapers seeking participants for a study of adolescent development (see Abela & Hankin, 2011). The final sample consisted of 382 adolescents (59% girls) and one parent (79% mothers) aged 11 to 15 years-old

($M = 13.04$, $SD = 1.11$) at the baseline assessment. The Montreal and Chicago samples were comparable in terms of adolescent sex, grade, highest level of maternal and paternal education, and family income ($ps > .05$). The Chicago sample consisted of a greater proportion of ethnic minority youth, $\chi^2(1) = 17.36$, $p < .001$, and youth from single-parent households, $\chi^2(1) = 8.84$, $p < .01$.

Procedures

The study consisted of a baseline laboratory assessment and then phone calls to complete questionnaire assessments every 3 months across 2 years following the initial assessment for a total of nine measurement time-points. Anxiety symptoms were not assessed at baseline, so our analyses focused on the second through ninth waves of assessment (hereafter referred to as Waves 1 through 8) for a total of 8 time-points. Youth and a parent completed questionnaires assessing the youth's symptoms of depression and anxiety and experience of SLEs at each time point. As reported in [Technow, Hazel, Abela, and Hankin \(2015\)](#), the average number of follow-up assessments completed by participants was 6.74 ($SD = 1.61$). Non-Hispanic White youth completed more follow-ups ($M = 7.4$, $SD = .13$) than other youth ($M = 6.1$, $SD = .22$), $t(345) = 5.33$, $p < .01$, and there was a moderate association between family income and completed follow-ups, $r = .18$, $p < .01$. The number of follow-up assessments completed was not significantly associated with youth's age, sex, depression or anxiety symptoms, and SLE exposure at baseline ($ps > .05$).

Measures

Psychopathology.

Depression. Depression symptoms were measured with the 27-item Children's Depression Inventory (CDI; [Kovacs & Staff, 2003](#)). Youth were asked to report on depression symptoms occurring in the last 2 weeks. Items are scored from 0 to 2 with higher scores indicating greater symptom severity. The CDI has good reliability and validity ([Craighead, Smucker, Craighead, & Ilardi, 1998](#)) and excellent internal consistency across all time points in the current study ($\alpha = .87-.91$).

Anxiety. Anxiety symptoms were measured with the 39-item Multidimensional Anxiety Scale for Children (MASC; [March, Sullivan, & Parker, 1999](#)). Youth were asked to report on anxiety symptoms occurring in the last 3 months. Items are scored from 1 (*never*) to 4 (*often*) with higher scores indicating greater symptoms severity. The MASC has good reliability and validity ([Muris, Merckelbach, Ollendick, King, & Bogie, 2002](#)). The MASC demonstrated good internal consistency across all time points in the current study ($\alpha = .72-.75$).

Stressful life events. SLEs were measured with the 57-item Adolescent Life Events Questionnaire (ALEQ; [Hankin & Abramson, 2002](#)). The ALEQ measures the occurrence of a broad range of negative events that typically occur among youth, including school, friendship, romantic, and family events. Youth were asked to report how often a stressor occurred within the last 3-months on a scale of 1 (*never*) to 5 (*almost always*). We used the total ALEQ score for the stress sensitization analyses. Based on prior work on internalizing psychopathology and stress generation that has observed stress generation effects primarily in the interpersonal domain ([Hammen, 2006](#); [Liu & Alloy, 2010](#); [Rudolph, 2008](#)), we

calculated a dependent-interpersonal ALEQ score for stress generation analyses (see the [online supplemental material](#) and [Hankin et al., 2010](#), for a full description of item coding methods). Scores were summed with higher scores indicating greater frequency of SLEs for both total and dependent-interpersonal ALEQ variables.

Statistical Approach

We were interested in examining (a) between- and within-person effects of SLEs on the trajectories of depression and anxiety symptoms (i.e., stress sensitization effects) and (b) between- and within-person effects of depression and anxiety symptoms on the trajectory of SLEs (i.e., stress generation effects) across 2 years (eight waves of data). We used multilevel models to examine these aims because they estimate parameters using all available Level 1 data (i.e., repeated assessments of participants over time), do not require all participants to have identical or balanced observations at Level 1, and permit examination of between- and within-person components of variance (and their interaction) in predictors and outcomes ([Raudenbush & Bryk, 2002](#)). We tested our hypotheses in R 3.3.1 using the package 'lme4' (Version 1.1-18-1 ([Bates, Mächler, Bolker, & Walker, 2014](#))). Model comparison was conducted using the maximum likelihood estimator (ML) to allow for comparison of models with different fixed effects specifications; final presented models estimated with restricted maximum likelihood estimator (REML) to reduce bias in random effects estimations ([Tom, Bosker, & Bosker, 1999](#)).¹

To separate the between- and within-person effects in stress sensitization and stress generation models, we used within-individual centering (i.e., centering each participant's observations at Level 1 around their person-specific mean across the 2-year study period) and grand-mean centering at Level 2 (i.e., centering each participant's mean level for the entire study period relative to the overall mean for the entire sample) for all predictors (i.e., total SLEs for stress sensitization and anxiety or depression symptoms for stress generation models). This approach entirely partitions variation in a given predictor into between- and within-person variability ([Enders & Tofighi, 2007](#)). In addition, we mean centered age and time so all intercept analyses are referring to the mean age of the sample (i.e., 13.04) and the midpoint of the study (i.e., between Waves 4 and 5), respectively. At each time point, stress and anxiety were assessed over the past three months, and depression over the last 2 weeks. To model prospective stress generation, depression and anxiety at the previous wave (i.e., 3 months earlier) were entered as predictors of current SLEs in stress generation models.

We examined stress sensitization and stress generation effects separately in depression and anxiety. While there is high diagnostic comorbidity between depression and anxiety across the life span ([Kessler et al., 2003](#)), several multiwave longitudinal studies have demonstrated that depression and anxiety can be partitioned into both shared and unique components with distinct trajectories as opposed to being represented by a single underlying internalizing factor ([Fergusson, Horwood, & Boden, 2006](#); [Olino, Klein, Lewinsohn, Rohde, & Seeley, 2008, 2010](#)).

¹ Final models estimates were nearly identical when using ML instead of REML. Summaries of our final models as estimated by ML are included in the [online supplemental material](#).

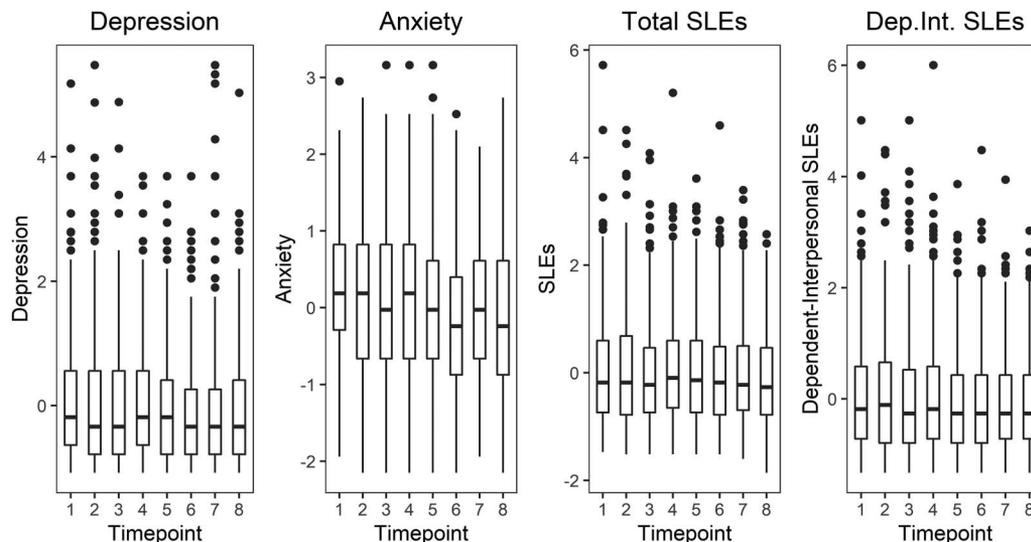


Figure 1. Unconditional growth models. Depression and anxiety symptoms and stressful life events (total and dependent-interpersonal) over time. Dep. Int. Stress = dependent-interpersonal stress.

We followed a standard model fitting approach. For all model comparisons we used $-2 \log$ likelihood and Akaike information criteria as tests of relative model fit (Raftery, 1995). We first estimated unconditional growth models for outcome variables (i.e., depression and anxiety symptoms or SLEs) to determine the shape of change over time, comparing different time functions and testing for random effects of time. Next, we examined main effects of covariates (age and gender) on each outcome. In the stress sensitization models, we then examined the effects of between- and within-person SLEs on anxiety and depression symptom outcomes. Specifically, we tested the hypothesis that within-person increases in SLEs (i.e., greater SLE exposure at a given point in time relative to one's mean level of SLE exposure) would be associated with greater depression and anxiety symptoms among youth who experience higher levels of SLEs on average than among youth with lower mean levels of exposure to SLEs. Stress generation models were similarly tested, but with between- and within-person main effects of anxiety and depression symptoms as predictors of SLEs. We hypothesized that youths who experienced an increase in depression or anxiety symptoms relative to their own average level of symptoms would be significantly more likely to report exposure to SLEs at that time point.

As recommended best practice for regression model building (Allison, 1977), we tested all covariate by predictor interactions to ensure that our primary analyses of interest were not biased by unmodeled dependencies in the data.² Specifically, simulations have demonstrated that neglecting to include or estimate interactions in models can induce substantial bias in the main effects of coefficients (Vatcheva, Lee, McCormick, & Rahbar, 2015). We refrained from interpreting any interactions to avoid capitalizing on chance and nonhypothesized effects.

In the service of transparency and reproducibility, we provide the statistical code used to generate all multilevel model analyses and the output as [online supplemental material](#) to the article.

Details of model validation can be found in the [online supplemental material](#).

Results

Descriptive Statistics

The distribution of depression and anxiety symptoms and frequency of SLEs across the eight waves of data are presented in [Figure 1](#). The correlation between demographic covariates, SLEs, and depression and anxiety symptoms is presented in [Table 1](#).

Unconditional Models

Unconditional growth models for depression and anxiety symptoms and dependent-interpersonal SLEs are presented in the [online supplemental material](#) ([Table 2](#), [Figure 1](#)).

Stress Sensitization

Main effects of SLEs predicting depression symptoms. We examined the between- and within-person associations of SLEs with depression symptoms over time, predicting the intercept and growth of depression symptoms from between- and within-person variability in exposure SLEs. The best fitting model demonstrated significant within- ($\beta = .31$, $SE = .01$, $p < .001$) and between-person ($\beta = .62$, $SE = .03$, $p < .001$) associations of SLEs with the level of depression symptoms at the midpoint of the study (but not the linear or quadratic effect of time), as well as an interaction between within-person SLEs and the linear effect of time ($\beta = .03$, $SE = .005$, $p < .001$). In other words, adolescents who experienced a higher average number of SLEs had higher levels of depression symptoms than adolescents who had a lower average

² Results were virtually unchanged when adding covariate by predictor interactions into final models.

Table 2
Unconditional Growth Models for Depression and Anxiety Symptoms and Stressful Life Events (SLEs)

Variable	β	Variance	SE	SD	LCL	UCL	<i>p</i>
Depression							
Fixed effects							
Intercept	.03		.05		-.06	.12	.557
Linear time	-.01		.008		-.03	.005	.178
Residual	-.003		.003		-.009	.003	.331
Random effects							
Intercept		.67		.82			
Linear time		.01		.11			
Quadratic time		.001		.03			
Residual		.36		.60			
Anxiety							
Fixed effects							
Intercept	.01		.05		-.09	.11	.820
Linear time	-.05		.01		-.06	-.03	<.001
Random effects							
Intercept		.63		.79			
Linear time		.006		.08			
Residual		.32		.57			
Dependent-interpersonal SLEs							
Fixed effects							
Intercept	.04		.05		-.05	.13	.425
Linear time	-.01		.007		-.02	.008	.382
Random effects							
Intercept		.69		.83			
Linear time		.01		.08			
Residual		.30		.55			

Note. LCL = lower confidence limit; UCL = upper confidence limit. Depression measured with the Children's Depression Inventory. Anxiety measured with the Multidimensional Anxiety Scale for Children. SLEs measured with the Adolescent Life Events Questionnaire.

number of SLEs (between-person effect) but exhibited no differences in the rate of change in depression symptoms over time. Moreover, the within-person association between SLEs and depression symptoms increased over time (within-person effects). There were no significant effects of between-person SLEs on linear or quadratic symptom growth and no effect of within-person SLEs on quadratic symptom growth; adding these terms to the model significantly worsened model fit across all indices.

Main effects of SLEs predicting anxiety symptoms. We examined the between- and within-person associations of SLEs with anxiety symptoms over time, predicting the growth and level of anxiety symptoms from between- and within-person variability in the frequency of SLEs. The best fitting model included significant within-person ($\beta = .21$, $SE = .02$, $p < .001$) and between-person ($\beta = .38$, $SE = .05$, $p < .001$) associations of SLEs with anxiety symptoms. There were no significant interactions of between- or within-person SLEs on linear symptom growth; adding these terms to the model significantly worsened model fit across all indices.

Stress sensitization predicting depression symptoms. We tested for stress sensitization effects in predicting depression symptoms by determining whether the association of within-person variability in SLEs on depression symptoms differed depending on the individual's overall mean level of SLE across all eight waves of data (i.e., between-person variability in SLEs). We tested this hypothesis by including a within-person SLE by between-

person SLE interaction variable as a predictor of depression symptoms. Table 3 presents these final results and Figure 2 visualizes these findings. We found significant moderation of within-person SLEs by between-person SLEs such that individuals with higher overall levels of SLEs across the entirety of the study experienced more depression symptoms at time points when they reported greater SLEs compared to their own average ($\beta = .02$, $SE = .01$, $p = .017$) relative to adolescents who had lower average levels of SLEs over the study period.

Stress sensitization predicting anxiety symptoms. We evaluated stress sensitization effects in predicting anxiety using the same approach (i.e., including a within-person SLE by between-person SLE interaction variable as a predictor of anxiety symptoms). We found no moderation of within-person variability by between-person variability in SLEs on anxiety symptoms (see Figure 2) and the addition of this interaction to the model significantly worsened model fit across all indices. Therefore, we removed the interaction term from the final model, and Table 3 presents these results.

Stress Generation

Depression symptoms predicting SLEs. We added the main effects of between-person depression and within-person deviations in depression symptoms from the previous wave as well as interactions with all other predictors to predict dependent-interpersonal SLEs. The best fitting model included significant main effects of between-person depression ($\beta = .42$, $SE = .04$, $p < .001$) and within-person depression assessed at the prior wave ($\beta = .03$, $SE = .02$, $p = .042$) in predicting exposure to SLEs and a significant two-way interaction between linear time and within-person depression symptoms ($\beta = -.03$, $SE = .009$, $p = .004$). The interaction indicated that the association between within-person increases in depression symptoms at the previous wave and exposure to dependent-interpersonal SLEs was strongest at the beginning of the study and became weaker over time (Supplemental Figure S1 in the online supplemental material). Table 4 presents the final results and Figure 3 visualizes the hypothesized main effect of between- and within-person depression symptoms in predicting greater SLEs.

Anxiety symptoms predicting SLEs. Similar to the depression and stress generation models, we systematically added the main effects of between-person and time-lagged within-person differences in anxiety symptoms as well as interactions with all other predictors to predict dependent-interpersonal SLEs. The best fitting model included significant main effects of between-person ($\beta = .38$, $SE = .05$, $p < .001$), but not within-person ($\beta = .002$, $SE = .01$, $p = .890$) differences in anxiety symptoms in predicting SLEs. Table 4 presents the final results and Figure 3 visualizes the main effect of between-person increases in anxiety symptoms predicting greater SLEs.

Discussion

Although theoretical models of the association between SLEs and internalizing psychopathology focus on within-person effects, previous research has primarily utilized cross-sectional designs and between-person analytic methods. The present investigation addressed this gap, demonstrating cumulative and bidirectional

Table 3
Stress Sensitization: Between and Within-Person SLEs Predicting Depression and Anxiety Symptoms (Final Models)

Variable	β	Variance	SE	SD	LCL	UCL	<i>p</i>
Depression							
Fixed effects							
Intercept	-.05		.04		-.14	.03	.228
Age	.008		.03		-.04	.06	.767
Sex	.11		.05		.005	.21	.040
Linear time	-.0003		.007		-.01	.01	.970
Quadratic time	.002		.002		-.003	.007	.369
Within-person SLEs	.30		.01		.27	.32	<.001
Between-person SLEs	.62		.03		.57	.67	<.001
Between-Person SLEs \times Within-Person SLEs	.02		.01		.004	.04	.017
Linear Time \times Within-Person SLEs	.03		.005		.02	.04	<.001
Random effects							
Intercept		.22		.47			
Linear time		.01		.09			
Quadratic time		.0002		.01			
Residual		.27		.52			
Anxiety							
Fixed effects							
Intercept	-.18		.07		-.32	-.05	.013
Linear time	-.04		.009		-.06	-.02	<.001
Age	-.03		.05		-.12	.06	.525
Sex	.40		.09		.22	.57	<.001
Within-person SLEs	.21		.02		.17	.25	<.001
Between-person SLEs	.38		.05		.29	.47	<.001
Random effects							
Intercept		.45		.67			
Linear time		.006		.08			
Residual		.29		.54			

Note. SLEs = stressful life events; LCL = lower confidence limit; UCL = upper confidence limit. Depression measured with the Children's Depression Inventory. Anxiety measured with the Multidimensional Anxiety Scale for Children. SLEs measured with the Adolescent Life Events Questionnaire.

associations between SLEs and symptoms of depression and anxiety in a 2-year prospective, multiwave study of adolescents. Our results support and extend prior work on the stress sensitization hypothesis, demonstrating that the association between recent SLEs and depression symptoms is stronger among adolescents who experience higher average levels of SLEs. The stress sensitization effect was specific to within-person variation in SLEs, meaning that depression symptoms were more likely to occur on months when an adolescent experienced greater exposure to SLEs than was typical for them, with a stronger within-person association among adolescents with greater overall exposure to SLEs during the study period. We additionally extended prior work on stress generation that has largely relied on between-person approaches, demonstrating associations of within-person depression symptoms and dependent-interpersonal SLEs, such that adolescents reported a greater number of dependent-interpersonal SLEs after experiencing higher levels of depression symptoms at the previous wave than is typical for them, and this effect was strongest at the beginning of the study. We found evidence for between-person, but not within-person, effects of anxiety symptoms on the generation of dependent-interpersonal SLEs. All effects were robust to the inclusion of covariate (i.e., age and gender) by predictor interactions, replication with multiple imputation, and model validation using SEM-based latent growth models with structured residuals (Curran, Howard, Bainter, Lane, & McGinley, 2014).

We provide novel evidence for the presence of stress sensitization effects in relation to normative SLEs occurring during adolescence. Specifically, we observed that depressive symptoms were higher on months when adolescents reported higher total SLEs than usual relative to their own average, and that this within-person association was significantly stronger among youth who had higher average levels of exposure to SLEs over the 2-year study period. This finding is consistent with the prior stress sensitization literature (e.g., Hammen et al., 2000; McLaughlin, Conron, et al., 2010) and extends these prior findings in several important ways. First, although theoretical models of stress sensitization inherently require within-person statistical approaches, previous research in children and adolescents has almost exclusively used either cross-sectional designs (Harkness et al., 2006) or between-person statistical approaches with longitudinal data (Espejo et al., 2007; Starr et al., 2014). The present study provides an important test of the stress sensitization hypothesis using a within-person statistical approach. Second, previous stress sensitization research has been conducted largely in adults (Hammen, 2006; Hammen et al., 2000; McLaughlin, Conron, et al., 2010; Wichers et al., 2009) or older adolescents (Shapiro et al., 2014; Starr et al., 2014). The two studies among youth samples were either cross-sectional (Harkness et al., 2006) or two-time point designs (Espejo et al., 2007) that do not allow for examination of individual fluctuations in SLEs and symptoms over time. Finally, we exam-

Stress Sensitization

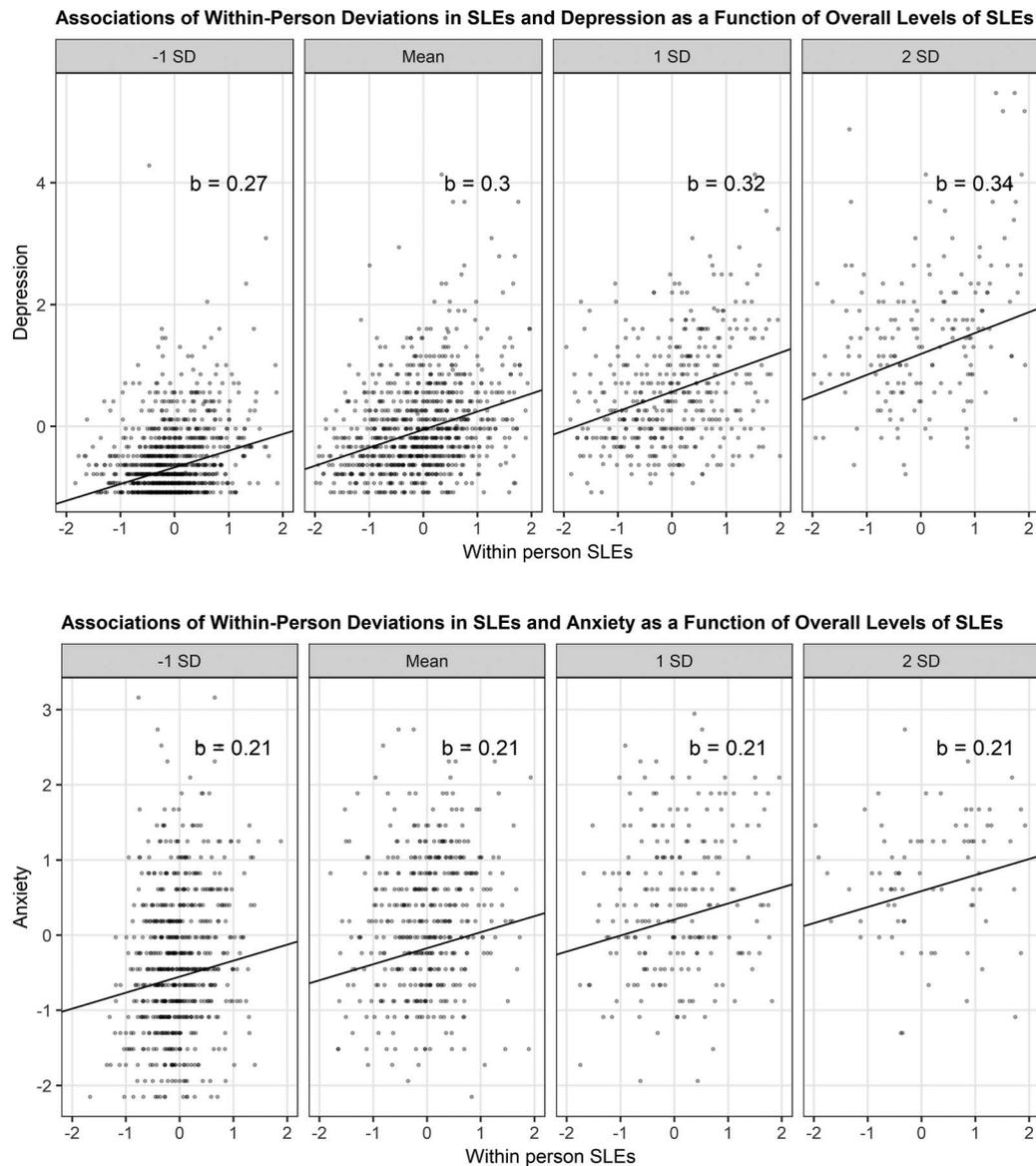


Figure 2. Stress sensitization effects. Effect of within-person centered (i.e., an individual's month to month variation) stressful life events on depression and anxiety symptoms at different levels of grand mean centered stress (i.e., an individual's average levels compared to the entire sample average). Annotated slopes were calculated by regressing the symptom levels predicted by the final models for each data point with within-person stressful life events (SLEs) for each level of between-person SLEs.

ined stress sensitization following the experience of relatively normative forms of SLEs as opposed to more severe forms of adversity, like maltreatment or exposure to violence (Hammen et al., 2000; McLaughlin, Conron, et al., 2010). The present study makes an important contribution by expanding the stress sensitization framework to adolescents reporting less severe forms of SLEs and suggests that exposure to a wide range of stressors can heighten vulnerability to depression and anxiety following SLEs occurring at a later point in time. Identifying the mechanisms that

underlie this type of stress sensitization, particularly using within-person modeling approaches, is an important goal for future research.

Although we found main effects for both between- and within-person SLEs predicting anxiety symptoms, we did not observe stress sensitization effects in relation to anxiety. This finding was contrary to our hypotheses and two previous studies examining stress sensitization in relation to childhood adversity and the association between SLEs and anxiety in adolescence (Espejo et

Table 4
Stress Generation Effects: Depression and Anxiety Symptoms Predicting Dependent-Interpersonal SLEs (Final Models)

Variable	β	Variance	SE	SD	LCL	UCL	<i>p</i>
Depression predicting SLEs							
Fixed effects							
Intercept	-.007		.06		-.13	.12	.913
Age	.12		.04		.04	.20	.005
Sex	.06		.08		-.10	.23	.448
Linear time	-.01		.008		-.03	.007	.252
Within-person depression	.03		.02		.001	.07	.042
Between-person depression	.42		.04		.33	.50	<.001
Linear Time \times Within-Person depression	-.03		.009		-.04	-.008	.004
Random effects							
Intercept		.53		.73			
Linear time		.009		.09			
Residual		.27		.52			
Anxiety predicting SLEs							
Fixed effects							
Intercept	.05		.07		-.09	.20	.470
Age	.16		.04		.07	.25	<.001
Sex	-.13		.09		-.31	.06	.180
Linear time	-.009		.01		-.03	.01	.388
Within-person anxiety	.002		.01		-.03	.03	.890
Between-person anxiety	.38		.05		.28	.47	<.001
Random effects							
Intercept		.53		.73			
Linear time		.01		.10			
Residual		.21		.46			

Note. SLEs = stressful life events; LCL = lower confidence limit; UCL = upper confidence limit. Depression measured with the Children's Depression Inventory. Anxiety measured with the Multidimensional Anxiety Scale for Children. SLEs measured with the Adolescent Life Events Questionnaire.

al., 2007) and adulthood (Hammen et al., 2000; McLaughlin, Conron, et al., 2010). This discrepancy might be related to the type of stressors assessed across studies. Specifically, both previous studies investigated more severe forms of environmental adversity and major life events (i.e., parental death, child maltreatment) as

opposed to the more normative types of SLEs examined here. Although it is important to not overinterpret a null finding, the discrepancy between the present study and past research may suggest that stress sensitization processes in relation to anxiety are applicable only among individuals who have experienced severe

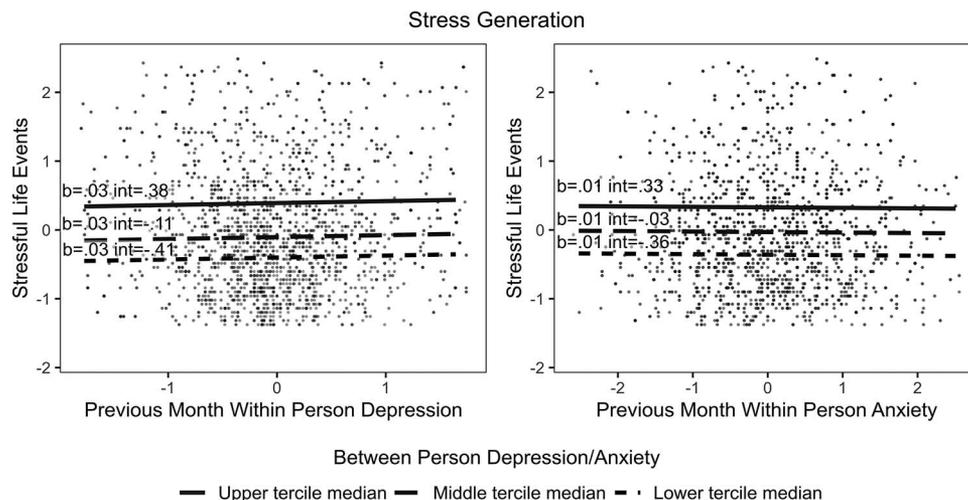


Figure 3. Stress generation effects. Main effects of within-person centered (i.e., an individual's month to month variation) and grand mean centered (i.e., an individual's average levels compared to the entire sample average) depression and anxiety symptoms on stressful life event exposure. Int = intercept.

adversities or major life events in childhood. Greater research is needed to explore this possibility in other samples.

We also examined whether the well-replicated bidirectional associations between SLEs and internalizing psychopathology from between-person designs would be observed in our within-subject approach. To do so, we evaluated whether adolescents reported an increased number of dependent-interpersonal SLEs after experiencing higher levels of depression or anxiety at the previous wave than was typical for them. We found evidence for this pattern of within-person stress generation for depression symptoms, and this effect was strongest earlier in the study period. Although we did not observe within-person effects of anxiety symptoms on the generation of dependent-interpersonal SLEs, we did find between-person effects of anxiety symptoms. These findings are broadly consistent with the extant stress generation literature in adolescents examining between-person differences in anxiety (McLaughlin & Nolen-Hoeksema, 2012) and depression (Hammen, 2006; Rudolph et al., 2009) in predicting exposure to SLEs. These between-person differences likely reflect a variety of trait-like differences among adolescents who develop depression and anxiety relative to those that do not, including neuroticism (Kendler, Kuhn, & Prescott, 2004; Muris, Roelofs, Rassin, Franken, & Mayer, 2005). Although there has been extensive replication of these between-person stress generation findings across the life-course, only one prior study used a within-subject approach to examine these associations in adolescents (Shapero et al., 2013), and this study was limited to a 5-month time frame with a sole focus on depression symptoms. Our findings that when adolescents experience greater levels of depressive symptoms than is typical for them, they are more likely to generate interpersonal stressors in their lives, together with this prior study, highlight the importance of identifying mechanisms underlying these within-person associations. Several candidate mechanisms that likely fluctuate along with symptoms of depression include difficulties with interpersonal problem-solving (Davila, Hammen, Burge, Paley, & Daley, 1995), avoidant coping strategies (Holahan, Moos, Holahan, Brennan, & Schutte, 2005), self-criticism (Shahar & Priel, 2003; Shih et al., 2009), and engagement in rumination and other maladaptive emotion regulation strategies (Kercher & Rapee, 2009; McLaughlin & Nolen-Hoeksema, 2012). Future studies using prospective, multiwave data are necessary to evaluate these potential within-person mechanisms.

Limitations of the current study include the use of self-report for measurement of depression and anxiety symptoms and exposure to SLEs over time. Although self-report measures used in the present study were well-validated, reliable assessments of internalizing psychopathology symptoms and a broad range of SLEs typically experienced by youth and allow for more frequent, long-term assessment of constructs, the use of interview-based measures would have been preferable. This is particularly important when considering mood-related memory biases in the reporting of SLEs (Mineka & Nugent, 1995; Teasdale, 1983), shared method variance, intracategory variability (Dohrenwend, 2006), and distinguishing between SLE occurrence and psychopathology-related responses to SLEs (Harkness & Monroe, 2016), which are mitigated with the use of contextual threat interviews (i.e., Hammen & Rudolph, 1999). Relatedly, we aggregated the prospective self-report of SLEs to evaluate how between-person effects of SLE exposure function as a moderator in stress sensitization models as

opposed to asking adolescents to retrospectively report their normative SLE exposure across the last few years at the first time-point. This method makes an assumption that youth who experienced globally higher levels of SLEs over the 2-year assessment period were likely to have also had higher rank-order exposure to SLEs prior to the study. Although there is evidence for continuity over time in the rank-ordering of exposure to SLEs among children and adolescents (e.g., Hanson et al., 2010; Pearlin, 1989; Raposa, Hammen, Brennan, O'Callaghan, & Najman, 2014), it is unknown whether this is an accurate assumption without having retrospective measurements of past SLE experiences and may temper inferences that can be drawn from the present study. Further, our focus on internalizing symptoms limits our ability to draw conclusions about how stress sensitization and generation processes may relate to clinical levels of internalizing psychopathology. Although many have advocated for dimensional approaches when assessing psychopathology to better assess severity, subclinical symptom presentations that may predict later disorder onset, and changes in symptoms over time (Kessler, 2002; Lebeau et al., 2012), the addition of a diagnostic assessment would strengthen clinical implications of future research. Finally, we examined stress sensitization and generation effects separately for depression and anxiety. Investigating the degree to which stress generation and sensitization processes are transdiagnostic across internalizing problems or specific to anxiety or depression remains an area for future research given the high diagnostic comorbidity, particularly at the symptom level (Kessler et al., 2003).

The present study advances understanding of stress sensitization and generation processes during adolescence by using a prospective, multiwave design and within-person analytical approach to examine cumulative and bidirectional associations between SLEs and internalizing psychopathology. We extend prior work on stress sensitization by documenting within-person sensitization effects following normative experiences of SLEs as compared to prior work examining severe forms of early adversity and between-person effects. Similarly, we document within-person stress generation effects, such that adolescents experiencing higher depression symptoms than is typical for them also reported higher levels of SLEs. Clinical implications of findings include the use of an individualized intervention approach in which adolescents may be at greater risk for symptom deterioration following particularly stressful months.

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