An Evaluation of Perceived Health Risk and Depressive Symptoms Before a Disaster in Predicting Postdisaster Inflammation

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ABSTRACT

Objective: Exposure to major life stressors is associated with subsequent enhanced inflammation-related disease processes. Depressive symptoms exacerbate stress-induced inflammatory responses. Moreover, those who report a high degree of perceived health risk before being exposed to a major life stressor such as a disaster are at risk for poor health outcomes. The present study examined whether perceived health risk and depressive symptoms before a disaster were associated with postdisaster inflammation markers.

Methods: The sample included 124 participants (mean [standard deviation] age = 55 [16] years; 69% women). At a baseline visit, participants completed self-report measures of perceived health risk and depressive symptoms (Center for Epidemiologic Studies Depression Scale) in addition to a blood draw for the assessment of inflammation markers (C-reactive protein, tumor necrosis factor receptor 1, and interleukin 6). All participants lived near a large petrochemical complex where an unexpected explosion occurred. A second blood sample was obtained 2 to 6 months after the explosion.

Results: No significant differences in inflammation markers were found between predisaster and postdisaster assessment ($p > .21$). An interaction between predisaster perceived health risk and depressive symptoms in predicting postdisaster circulating inflammation markers was identified (Cohen $f^2 = 0.051$). Specifically, predisaster perceived health risk was associated with postdisaster circulating inflammation markers if predisaster depressive symptoms were greater than 8.10 on the Center for Epidemiologic Studies Depression Scale.

Conclusions: These findings add to our understanding of the complex interactions between stress, depression, and immune responses. Indeed, findings provide a potential mechanism (i.e., inflammation) explaining the association between exposure to major life stressors and negative mental and physical health outcomes.

Key words: psychoneuroimmunology, depression, stress, proinflammatory cytokines, environmental hazards, health risk.

INTRODUCTION

People who experience frequent high stress are at increased risk for poor mental and physical health outcomes in comparison to those who experience less stress. One mechanism through which stress is associated with mental and physical health outcomes is the up-regulation of inflammation. Indeed, inflammation is implicated in the onset and progression of many diseases associated with poor well-being (1–3) in addition to morbidity and mortality (4). Stressful life events and the negative emotions they generate are reliably associated with increased circulating markers of inflammation (5). The present study sought to identify prospective predictors of inflammation after exposure to a stressful life event using a novel design where inflammation was assessed before and after an industrial accident.

The cognitive activation theory of stress (CATS) (6) suggests that prior stressful experiences prime an individual's psychological and physiological responses to stressful situations. Therefore, if an individual experiences heightened stress, that individual is more likely to experience high stress in future situations. In line with the CATS, depressive symptoms sensitize future inflammatory responses to stress (7–9). For instance, those with a history of depressive symptoms who were exposed to an acute laboratory stressor demonstrated increased circulating markers of inflammation in comparison to those without a history of depressive symptoms (10). Furthermore, women with a lifetime history of depression demonstrated increased circulating markers of inflammation after childbirth in comparison to those without a history of depression (11). In addition to major depression, recent work suggests that even mild to moderate levels of depressive symptoms prime inflammatory responses. Indeed, mild depressive symptoms were associated with increased circulating markers of inflammation after influenza vaccination (7).

CATS = cognitive activation theory of stress, **COV** = coefficient of variation, **CRP** = C-reactive protein, **IL-6** = interleukin 6, **LOD** = limit of detection, **TNF-α** = tumor necrosis factor α, **TNF-r1** = tumor necrosis factor receptor 1

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Research studies evaluating the role that depressive symptoms play in provoking human stress induced inflammation have focused on acute stressors. Unlike work in animal models that have induced prolonged stressors (12,13), there is no work examining this model in humans. To better understand how a history of depression differentially affects the stress-response system after a highly stressful life event (14,15), individuals need to be examined both before and after the stressful life event.

Industrial accidents are particularly impactful on physical and emotional health. Indeed, exposure to industrial accidents (hereafter referred to as "a disaster") was associated with mental and physical health problems in prior studies (16–20). According to the CATS, expectations for outcomes of potentially stressful experiences are important for determining psychological and physiological responses to them (6). Consistent with the CATS, those who perceive a high degree of risk for a future disaster in their community demonstrate prolonged stress responses due to fear of health problems and lack of control, among other variables, when faced with a disaster (21,22). Therefore, in addition to depression, the subjective expectation of harm before a disaster (i.e., predisaster perceived health risk) predicts how individuals respond after the disaster for prolonged periods. This is important given that chronic stress decreases the sensitivity of immune cells to glucocorticoid hormones (i.e., glucocorticoid resistance) that typically decrease acute inflammatory responses (23). Glucocorticoid resistance promotes enhanced duration and intensity of inflammatory responses to stress, leaving individuals susceptible to chronic inflammatory diseases such as cardiovascular disease and Type 2 diabetes (5). A better understanding of how predisaster variables such as perceived risk and depression are associated with postdisaster inflammation is needed to enhance our knowledge of the biobehavioral mechanisms linking exposure to disasters with health outcomes.

The present study sought to evaluate how predisaster perceived health risk and depressive symptoms were associated with immune dysregulation after exposure to a disaster. We expected that greater predisaster perceived health risk would be associated with higher postdisaster inflammation. Furthermore, given work indicating that depression primes the inflammatory stress response, we expected that predisaster depressive symptoms would change the association between predisaster perceived health risk and inflammation such that predisaster perceived health risk would be more strongly associated with postdisaster inflammation among those with high predisaster depressive symptoms. We expected that these hypothesized associations would be observed above and beyond predisaster inflammation, demographic characteristics of participants, and indicators of objective exposure to the disaster.

METHODS

Participants and Procedure

Data were obtained from the baseline and follow-up visits of the Texas City Stress and Health Study. The study was part of a larger project targeting health among Hispanic individuals by the Center for Population Health and Health Disparities. All participants ($N = 124$) were living in Texas City, Texas, before and after a petrochemical accident on March 23, 2005, in which 15 oil workers died and approximately 170 were injured due to a large explosion (19,24). The baseline visit occurred before the petrochemical accident and the follow-up visit occurred between May and August 2005 (2–6 months after the explosion), allowing for examination of prospective predictors of postdisaster inflammation. Visits were rescheduled if the participant demonstrated, or self-reported, symptoms of acute illness at the initiation of the visit. The study protocol was approved by the University of Texas Medical Branch institutional review board, and informed consent was obtained from all participants.

At the baseline and follow-up visits, a trained phlebotomist drew blood between 9 AM and noon in the morning. Blood was collected either at the participant's household or at a centrally located clinic in Texas City, Texas. Participant blood samples were centrifuged to obtain plasma and were batch analyzed to reduce the likelihood of variation between assays (described in the following section).

Measures

Predisaster and Postdisaster Perceived Health Risk

Participants completed the Concern about Petrochemical Health Risk Scale (24), a four-item measure of one's subjective risk of health problems due to living near a petrochemical plant. The four items focus on concerns of health risks stemming from pollution, accidents, stored waste, and general health risks from oil and chemical industries in close proximity. Participants were asked to indicate their degree of concern for each item on a scale ranging from 1 (not at all concerned) to 5 (extremely concerned). Items were summed to form an overall score. Internal consistency was excellent for the Concern about Petrochemical Health Risk Scale both before ($\alpha = .98$) and after the disaster ($\alpha = .97$). Postdisaster perceived health risk was used as a covariate.

Predisaster Depressive Symptoms

The Center for Epidemiologic Studies Depression Scale–Revised (25) was used as an indicator of predisaster depressive symptoms. Participants were asked to complete the 20-item Center for Epidemiologic Studies Depression Scale–Revised while referencing symptoms of depression they had experienced during the prior 2 weeks on a scale ranging from 0 (rarely) to 3 (most or all of the time). A continuous variable, as opposed to a clinical cutoff, was used in the analyses described in the analytic strategy section. Depressive symptoms were not measured after the disaster. Internal consistency for predisaster depressive symptoms was excellent ($\alpha = .90$), and scores ranged from 0 to 58.

Predisaster and Postdisaster Inflammation

Enzyme-linked immunosorbent assays were used to measure C-reactive protein (CRP), interleukin 6 (IL-6), and tumor necrosis factor receptor 1 (TNF-r1). A commercially available kit was used to measure CRP (high sensitivity; Diagnostic Systems Laboratories, Webster, TX; limit of detection [LOD], 0.1 mg/L; coefficient of variation [COV], <5%). IL-6 was measured using OptEIA assay kits from BD Pharmingen (San Diego, CA; LOD, 2.2 pg/ml; COV, <10%), and TNF-r1 was measured using R&D Systems Duoset assay kits (Minneapolis, MN; LOD, 10 pg/ml; COV, <10%). Two quality controls (high and low levels) were included with all batches to assure the accuracy of the results, and the detected values for these controls fell within the expected range. TNF-r1 was used instead of tumor necrosis factor α (TNF-α), given that TNF-r1 is more easily detectable and TNF-α has a short half-life of approximately 15 minutes (26). Furthermore, TNF-r1 is a surrogate marker of TNF-α (27). Overall indicators of predisaster and postdisaster inflammation were calculated by *z* standardizing and combining each biomarker for each time point, which is consistent with the literature demonstrating the importance of cumulative inflammatory load/burden in predicting health-related outcomes (28).

Demographics

Self-reports of age, sex, and race/ethnicity were provided by participants during the baseline visit. Furthermore, participant height and weight were

measured at the baseline visit before blood was drawn to calculate a body mass index.

Exposure Variables

A number of variables reflecting exposure to the disaster were collected and used as covariates in the analyses described in the following section. First, geographical information system software was used to determine the shortest distance from each participant's home address to the isomerization unit at the refinery that exploded. Furthermore, during the postdisaster visit, participants provided self-reports of whether or not they heard or felt the explosion, in addition to whether or not they saw the smoke from the explosion.

Analytic Strategy

Confirmatory factor analyses were conducted using IBM SPSS AMOS software to confirm a single-factor structure for predisaster and postdisaster circulating markers of inflammation. Linear regression analyses using SPSS software (29) were used to examine predisaster depressive symptoms as a moderator of the association between predisaster perceived health risk and postdisaster inflammation (30). We adjusted for predisaster inflammation markers, body mass index, the number of days between the baseline assessment and the explosion, and the number of days between the explosion and the follow-up assessment, in addition to participant age, sex, race/ethnicity, household distance from the explosion, postdisaster perceived health risk, and whether or not they heard, saw, or felt the explosion. Furthermore, separate regression analyses were run analyzing whether or not each exposure variable interacted with predisaster depressive symptoms to predict postdisaster inflammation. Variables were mean centered before statistical analysis.

RESULTS

Descriptive statistics are provided in Table 1, and zero-order correlations are presented for primary study variables in Table 2. Predisaster IL-6 was associated with predisaster CRP (r = 0.21, p = .02) and TNF-r1 (r = 0.234, p = .009); predisaster CRP and TNF-r1 were also associated (r = 0.26, p = .004). Postdisaster IL-6 was associated with TNF-r1 (r = 0.26, p = .003) but not CRP (r = 0.10, p = .25); postdisaster CRP was associated with TNF-r1 (r = 0.22, p = .013). Predisaster depressive symptoms were associated with postdisaster IL-6 (r = 0.21, p < .05). Nonsignificant associations were identified between predisaster depressive symptoms and CRP (predisaster: r = 0.09, p = .31; postdisaster: r = 0.15, p = .10) and TNF-r1 (predisaster: r = 0.02, p = .82; postdisaster: r = 0.08, p = .36). Furthermore, predisaster perceived health risk was not significantly associated with IL-6 (predisaster: r = −0.02, p = .81; postdisaster: r = 0.07, p = .41), CRP (predisaster: r = 0.03, p = .76; postdisaster: r = 0.01, p = .89), or TNF-r1 (predisaster: r = 0.08, p = .36; postdisaster: r = −0.09, p = .32).

Separate confirmatory factor analyses were conducted to examine whether or not a single factor fit the data for predisaster and postdisaster circulating inflammatory markers. The results for predisaster circulating inflammatory markers indicated that a single factor was a good fit to the data (root mean square error of approximation, 0.03; 90% confidence interval, 0.01–0.04) (31). Similarly, a single factor represented a good fit to the data for postdisaster circulating inflammatory markers (root mean square error of approximation, 0.02; 90% confidence interval, 0.01–0.04). Standardized regression weights (i.e., factor loadings) were acceptable for both the predisaster (IL-6, 0.43; CRP, 0.48; TNF-r1, 0.54) and postdisaster (IL-6, 0.35; CRP, 0.30; TNF-r1, 0.75) factors (32). There were no significant differences between markers of inflammation before the disaster and those after the disaster using paired-sample t tests (p > .21).

TABLE 1. Participant Characteristics (N = 124)

Variable	Values
Age, M (SD), y	55.91 (16.10)
Sex, no. (%)	
Male	38 (31)
Female	86 (69)
Ethnicity, no. (%)	
Non-Hispanic white	38 (31)
US-born Hispanic	46 (37)
Foreign-born Hispanic	26 (21)
African American	14 (11)
Body mass index, M (SD), kg/m^2	30.92 (7.14)
Predisaster perceived health risk, M (SD)	6.13 (4.82)
Predisaster depressive symptoms, M (SD)	9.24 (10.77)
Predisaster inflammation, M (SD)	
C-reactive protein[a]	11.97 (12.71)
Tumor necrosis factor receptor 1[b]	1963.25 (1384.32)
Interleukin 6[b]	3.04 (6.34)
Postdisaster inflammation, M (SD)	
C-reactive protein[a]	12.06 (15.34)
Tumor necrosis factor receptor 1[b]	1910.10 (1370.61)
Interleukin 6[b]	2.36 (4.94)
Postdisaster perceived health risk, M (SD)	6.55 (4.78)
Days between baseline and explosion, M (SD)	100.86 (70.44)
Days since explosion at follow-up, M (SD)	69.19 (29.04)

[a] Units (mg/dl).
[b] Units (pg/ml).

Predisaster inflammation (r = 0.764, p < .001) and depressive symptoms (r = 0.21, p = .02), as well as whether or not individuals felt the explosion (r = 0.19, p = .04), were associated with postdisaster inflammation. In an unadjusted model, the interaction between perceived health risk and depressive symptoms was associated with postdisaster inflammation (B = 0.002, p < .001). We also evaluated an adjusted model, and the interaction between predisaster perceived health risk and depressive symptoms remained significant (see Table 3 and Fig. 1). Specifically, using the Johnson-Neyman technique (33), which identifies regions of significance in moderation analyses, predisaster perceived health risk was significantly associated with postdisaster inflammation if depressive symptoms were greater than but not less than 8.10 before the explosion (Cohen f^2 = 0.051). Thirty-five percent of the sample (n = 59) was above this cutoff for statistical significance. Nonsignificant findings were identified when examining the interaction between predisaster depressive symptoms and perceived health risk when predicting postdisaster IL-6 (B = 0.002, p = .80), CRP (B = −0.001, p = .34), and TNF-r1 (B = 0.001, p = .15). Furthermore, none of the exposure variables significantly interacted with depressive symptoms in predicting postdisaster inflammation (all p values ≥.727). In ancillary analyses adjusting for

TABLE 2. Pearson Correlations Between Study Variables

Variable	1	2	3	4	5	6	7	8	9	10	11	12	13
1. T1 perceived health risk	—												
2. T1 depressive symptoms	−0.13	—											
3. T2 inflammation	0.07	0.20*	—										
4. T1 age	0.10	−0.04	0.13	—									
5. Sex	−0.11	0.11	−0.06	−0.19*	—								
6. T1 body mass index	−0.07	0.06	0.14	−0.03	0.23*	—							
7. Distance from explosion	0.243**	0.12	−0.19*	0.12	−0.07	−0.07	—						
8. Heard explosion	−0.14	0.06	0.17	0.08	0.07	0.23*	−0.09	—					
9. Saw explosion	−0.11	0.12	0.01	−0.04	0.01	0.06	−0.14	0.528**	—				
10. Felt explosion	−0.16	0.11	0.19*	−0.06	0.05	0.16	−0.21*	0.765**	0.529**	—			
11. T2 perceived health risk	0.485**	−0.01	−0.18*	0.218**	−0.06	−0.11	0.13	−0.06	−0.13	−0.11	—		
12. T1 to explosion	−0.01	−0.17	−0.01	−0.01	−0.08	−0.08	0.08	0.01	−0.04	0.04	−0.04	—	
13. Explosion to T2	0.04	−0.04	0.18*	−0.243**	0.06	−0.16	−0.18*	−0.03	0.03	0.04	−0.07	0.12	—
14. T1 inflammation	−0.01	0.21*	0.764**	0.20*	−0.03	0.241**	−0.235**	0.287**	0.12	0.30**	−0.18*	−0.06	−0.02

T1 = predisaster (i.e., baseline); T2 = postdisaster; inflammation = *z* standardized and combined indicators of circulation C-reactive protein, interleukin 6, and tumor necrosis factor receptor 1 at each time point.

* $p < .05$, ** $p < .01$.

participant demographics, the interaction between predisaster perceived health risk and depressive symptoms was not associated with predisaster inflammation ($B = 0.002$, $p = .10$).

DISCUSSION

Present study findings indicate that predisaster perceived health risk and depressive symptoms interact to predict postdisaster

TABLE 3. Linear Regression Analysis Predicting Postdisaster Inflammation

Variable	*B*	SE	*p*	95% CI
Constant	0.24	0.35	.49	−0.45 to .93
Perceived health risk	−0.01	0.01	.41	−0.03 to 0.01
Depressive symptoms	−0.01	0.04	.74	−0.02 to 0.01
Perceived health risk by depressive symptoms	0.01	0.01	>.001	0.01 to 0.01
Age	0.01	0.01	.49	−0.01 to 0.01
Sex	−0.01	0.08	.28	−0.25 to 0.07
Body mass index	−0.01	0.01	.50	−0.02 to 0.01
Distance from isomerization unit	0.01	0.01	.33	−0.01 to 0.01
Heard explosion	0.03	0.15	.85	−0.27 to 0.33
Saw smoke from explosion	−0.23	0.12	.07	−0.47 to 0.02
Felt explosion	−0.05	0.15	.74	−0.33 to 0.23
Postdisaster perceived health risk	−0.01	0.01	.24	−0.03 to 0.01
Days from baseline to explosion	0.01	0.01	.49	−0.01 to 0.01
Days since explosion at follow-up	0.01	0.01	.005	0.01 to 0.01
Predisaster inflammation	0.68	0.07	>.001	0.55 to 0.81
F	18.13			
df	(14, 109)			
R^2	0.71			
ΔR^2	0.05		>.001	

ΔR^2 = the change in R^2 due to the inclusion of the interaction term.

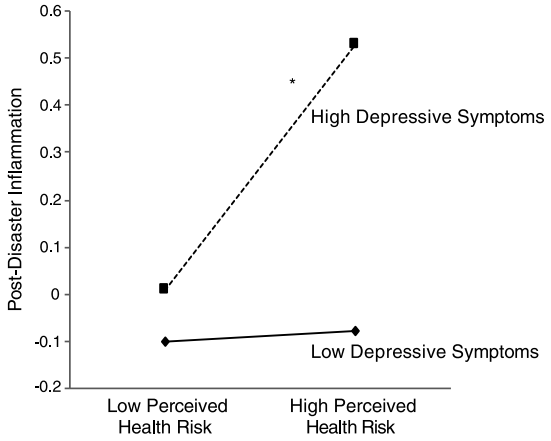

FIGURE 1. Postdisaster inflammation (i.e., *z* standardization and combination of the markers C-reactive protein, interleukin 6, and tumor necrosis factor receptor 1) at low (−1 standard deviation; standard error = 0.012) and high (+1 standard deviation; standard error = 0.013) perceived health risk and depressive symptoms (p interaction < 0.001; Cohen $f^2 = 0.051$).

inflammation such that those with higher perceived health risk were only vulnerable to higher inflammation if they also had higher predisaster depressive symptoms. Depressive symptoms are known to enhance stress-induced inflammatory responses (8), and the present study extends the literature by demonstrating the importance of depressive symptoms in predicting inflammatory responses to disasters. Perceived health risk has been linked to physical and emotional well-being after disasters (18,19), and our results indicate that depressive symptoms and inflammation may be important for understanding this link, although future studies are needed to test this possibility. In addition to morbidity and mortality (4,34), both stress and inflammation are associated with depression, cardiovascular disease, and some cancers (1–3,5).

These findings are in accord with animal work that demonstrated enhanced and prolonged inflammatory responses in rats and rhesus monkeys when confronted with stressful events (12), which sensitized them to future stress-induced inflammatory responses (13). Moreover, heightened inflammation has been observed in close temporal proximity to a stressor among humans with a history of depressive symptoms (7,8,10,11). Findings from the present study remained consistent when predisaster inflammation was included as a covariate, indicating that the residualized change in inflammation from predisaster to postdisaster was predicted by the synergistic association between perceived health risk and depressive symptoms. As a result, our findings are consistent with research demonstrating that prior stress and depression can enhance stress-induced inflammatory responses (10). Importantly, prolonged stress–induced inflammatory responses have detrimental mental and physical health consequences (8). It will be important to evaluate the time course of these associations in future work.

Objective indicators of exposure to a disaster were important for predicting postdisaster well-being in prior work. For instance, Peek et al. (19,35) identified evidence indicating that distance from an explosion and explosion impact (i.e., the degree to which individuals felt, saw, or heard the explosion) were important for predicting self-reported physical and mental health. Consistent with the CATS (6), our findings highlight the importance of subjective thoughts and feelings before a disaster in predicting postdisaster inflammation above and beyond objective indicators of exposure. Indeed, none of the exposure variables were associated with postdisaster inflammation when subjective variables were included in the analyses. Further research is clearly needed given that objective indicators of exposure have been associated with perceived health changes in the aftermath of disasters (36); however, most studies have focused on within-disaster and postdisaster variables given methodological concerns associated with collecting data before a disaster.

Our study did not identify the specific physiological processes that promoted inflammation among those with high predisaster perceived health risk and depressive symptoms. Both autonomic and neuroendocrine functioning may enhance stress-induced inflammation and should be included in future studies. Specifically, high parasympathetic activity is associated with reduced inflammation through the cholinergic anti-inflammatory pathway via the release of acetylcholine (37). Furthermore, norepinephrine is associated with enhanced inflammation through activation of nuclear factor κB transcription (38,39). Accordingly, future work would benefit from measuring parasympathetic activity and norepinephrine to generate a better understanding about how exposure to a disaster can lead to enhanced inflammation. Stress measurements were not included in the present study. Hypotheses were based on prior theoretical and empirical evidence indicating that exposure to disasters is associated with prolonged stress, especially among those who perceive a high degree of risk before exposure to the disaster (21,22). As a result, it would be beneficial to include stress measures throughout the predisaster and postdisaster periods to generate a better understanding of the role of stress and depressive symptoms in moderating biological responses to disasters.

Given the sample size of the present study, our limited statistical power did not allow us to examine if findings differed by race/ethnicity, which should be addressed in future research. As our sample largely reported Hispanic ethnicity, it is unclear if our findings would generalize to other populations. The lack of a control group, comprising those who were not exposed to the stressor, limits the ability to state that changes in circulating inflammatory markers were due to the explosion. Furthermore, future work may benefit from examining other factors that may influence circulating inflammation markers including chronic illnesses, injuries, medical procedures, medications, and tobacco and alcohol use.

Predisaster perceived health risk was not associated with postdisaster inflammation in the present study. Prior work indicated that predisaster perceived health risk was associated with postdisaster stress responses (18,19); however, such studies evaluated subjective stress responses as opposed to objective indicators such as inflammation. It is unclear why predisaster perceived health risk is associated with subjective, as opposed to objective, stress responses. As mentioned previously, we were unable to identify the time course of inflammatory responses to a disaster; however, findings provide initial evidence that predisaster perceived health risk and depressive symptoms are important in predicting inflammation 2 to 6 months after a disaster. Given that the follow-up visit was not conducted in close temporal proximity to the disaster, it is unclear if present study findings capture inflammatory reactivity to stress consistent with prior work (10). It would be beneficial to examine inflammatory responses soon after

exposure to a disaster in future studies. Furthermore, we were unable to determine causality for associations between predisaster and postdisaster perceived health risk, depressive symptoms, and inflammation given that depressive symptoms were not measured postdisaster. Future work would benefit from measuring depressive symptoms before and after individuals experience major life stressors to extend present study findings.

CONCLUSIONS

Individuals exposed to disasters are at risk for negative mental and physical health outcomes. This research demonstrates that predisaster perceived health risk and depressive symptoms interact to predict postdisaster inflammation. Specifically, predisaster perceived health risk was associated with postdisaster inflammation among those with high predisaster depressive symptoms. Accordingly, it would be beneficial to examine inflammation as a mechanism that may underlie the associations between exposure to disasters and negative mental and physical health outcomes in future work.

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