Journal of Traumatic Stress
June 2014, *27,* 345–352

ISTSS International Society for Traumatic Stress Studies

Inflamed by the Flames? The Impact of Terrorism and War on Immunity

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The physiological impact on citizens of prolonged exposure to violence and conflict is a crucial, yet underexplored, issue within the political science and biology literature. We examined the effect of high levels of exposure to rocket and terrorist attacks on biological markers of immunity and inflammation in a sample of 92 Israelis. A stratified random sample of individuals was drawn from a pool of subjects in Israel who had previously been interviewed regarding their stress exposure and psychological distress during a period of active rocket and terrorist attacks. These individuals were reinterviewed and blood samples were collected to assess antibodies to cytomegalovirus (CMV antibodies) and C-reactive protein (CRP). Posttraumatic stress disorder (PTSD) was significantly related to CRP, $\beta = .33$, $p = .034$, with body mass index, depression, and exposure to terrorism included in the model. Depression scores were not significantly associated with CRP or CMV antibody levels. In contrast to the established convention that psychological distress is the sole outcome of terrorism exposure, these findings reveal that individuals exposed to terrorism experience higher levels of both PTSD/depression, and inflammation. This study has important ramifications for how policy makers and medical health professionals should formulate public health policies and medically treat individuals living in conflict zones.

Understanding the health consequences of citizens' prolonged exposure to conflict violence is a crucial challenge for political science, trauma, and biology researchers (Boscarino, 2008; Canetti, Hall, Rapaport, & Wayne, 2013; Canetti, Rapaport, Wayne, Hall, & Hobfoll, 2013). Previous work demonstrated the impact of exposure on psychological distress and perceptions of threat in conflict zones (Canetti, Hall, et al., 2013; Canetti, Halperin, Sharvit, & Hobfoll, 2009). Understanding the health consequences of psychological stress has significant implications for the management, treatment, and progression of disease in individuals (McEwen, 1998; Terre, 2011; Wilkinson & Goodyer, 2011; Yehuda et al., 2009). Traumatic stressors including combat, terrorist attacks, rape, and disaster, and the resultant symptoms of posttraumatic stress disorder (PTSD) often associated with trauma have been linked to negative health consequences, including heart disease and cancer (Boscarino, 2008; Coussens & Werb, 2002; O'Toole & Catts, 2008; Sareen, Cox, Clara, & Asmundson, 2005). The process, however, by which traumatic stress produces these chronic diseases is often unclear or unexamined (Cohen, Marmar, Ren, Bertenthal, & Seal, 2009; McFarlane, 2010; Qureshi, Pyne, Magruder, Schulz, & Kunik, 2009).

Inflammation is an immune system response to infection or injury that rids the affected area of pathogens and facilitates wound and disease healing. Inflammation involves the production of proinflammatory cytokines including interleukin 6 (IL-6) and tumor necrosis factor (TNF), as well as acute phase reactants including C-reactive protein (CRP; Gouin, 2011). Paradoxically, inflammation, when prolonged, can be detrimental to health. Chronic, low-grade inflammation has been associated with cardiovascular disorders, diabetes, autoimmune disorders, and cancer in both epidemiological studies and experimental animal models (Aggarwal, Shishodia, Sandur, Pandey, & Sethi, 2006; Maggio, Guralnik, Longo, & Ferrucci, 2006).

This study was made possible, in part, by grants from the National Institute of Mental Health (R01 MH073687) and the Ohio Board of Regents. This work was supported by the following grants from the National Institute of Health and the National Institute of Mental Health: 1 R01 MH073587-01A2, Terrorism and Traumatic Responding: Exposure and Resiliency Factors; NIH-NHLBI 1P50HL105189, Rush Center for Urban Health Equity, and NIH RO1AT007 143, Biological and Psychological Factors as Predictors and Indicators of Mindfulness-Based Stress Reduction (MBSR) Response. We are grateful to Dennis Kahn for assistance with project coordination and data collection, Iris Lavi for assistance with data collection, Ori Rogowski (Souraski Medical Center) for orientation and supervision of the biological assays collection and data storage, and the Mahshov Research Institute for complex data collection amid ongoing conflict.

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DOI: 10.1002/jts.21920

Antibodies to cytomegalovirus (CMV) are a general indicator of immune dysregulation and the reactivation and proliferation of latent viruses. Chronic, latent viral infections are common, with the population prevalence of prior CMV infection estimated between 45%–100% depending on geographic region, and demographic factors (Cannon, Schmid & Hyde, 2010; de Jong et al., 1998; Henle & Henle, 1982). Cellular immune mechanisms control reactivation of latent CMV (Glaser, 2005; Glaser & Gotlieb-Stematsky, 1982; Henle & Henle, 1982), and stress-induced down regulation of these immune regulators can result in viral reactivation, which in turn results in renewed humoral responses to the pathogen. Reactivation can be assessed via antibody levels, with greater viral antibodies indicating downward regulation of cellular immunity. Reactivation of such latent infection has been shown to induce changes that could lead to atherosclerosis and plaque rupture, including endothelial smooth muscle cell proliferation, increased expression of proinflammatory cytokines with resulting T-cell migration into atherosclerotic plaques, and increased synthesis of coagulation factors (Epstein, Zhu, Najafi, & Burnett, 2009). Large, prospective studies of individuals with coronary artery disease have found seropositivity and higher viral antibody levels to be significantly associated with increased risk of myocardial infarction and death (Epstein et al. 2009; Espinola-Klein et al., 2002; Rupprecht et al., 2001).

In addition, CRP, an acute phase protein and a downstream marker of inflammation that is regulated by IL-6 and other proinflammatory cytokines, is associated with obesity, insulin resistance, and risk of cardiovascular disease (Hak et al., 1999). CRP is elevated in individuals with PTSD (Miller, Sutherland, Hutchison, & Alexander, 2001; von Känel et al., 2007) and has been suggested as a potential mediating mechanism in the link between PTSD and cardiovascular disease (Spitzer et al., 2010). At least one study, however, on Iraqi refugees found an association in the opposite direction, with lower CRP levels in individuals with PTSD (Söndergaard, Hansson, & Theorell, 2004). The current study expands on previous work by examining the relationship between war-related trauma, PTSD, depression, and biomarkers of immune dysregulation and inflammation. Israel provides an ideal context to study this question given the high rates of trauma in an active conflict zone.

Since the escalation of the Israeli–Palestinian conflict (Al-Aqsa Intifada) in 2000, Israeli citizens have been exposed to continuous threat of terror, characterized by missile attacks. During 2000–2009, 1,178 Israelis were killed in various types of terror attacks against civilians (Israeli Security Agency, 2010). Over 8,000 missiles were fired on Israel's cities and settlements, killing 32 Israelis. The rockets reached large cities in southern Israel, leading to significant life disruption. We hypothesized that reporting more symptoms of PTSD and depression would be associated with greater anti-CMV and CRP levels. As symptoms of PTSD and depression overlap and may additively describe individuals' distress, we examined both the individual and combined impact of PTSD and depression symptoms on anti-CMV and CRP levels. The analysis also considered unique impacts of these symptoms over and above demographic factors because biomarkers including CRP may vary across demographic factors including gender and age (Woloshin & Schwartz, 2005).

Method

Participants and Procedure

The study protocol was approved by the institutional review board at Rush University Medical Center. Participants were recruited from subject pools that had participated in previous large studies ($N = 840$ to 1,365) with our research group between the years 2007–2009 in Israel (Hobfoll, Hall, & Canetti, 2012; Lavi, Canetti, Sharvit, Bar-Tal, & Hobfoll, 2012; Palmieri, Chipman, Canetti, Johnson, & Hobfoll, 2010). Two potential groups were identified: (a) those in high terror-exposed regions who were also likely to be personally exposed to trauma; and (b) those in a nearby low terror-exposed region who were less likely to be personally exposed to trauma. From these two groups, equal numbers of individuals were randomly selected and contacted to ensure that we had chronically and personally exposed individuals, as well as individuals not exposed to trauma, our stratification factor.

The 1,149 potential participants were recontacted by telephone between October and November 2010. Participants were offered vouchers worth 100 Israeli new shekels (NIS; roughly 30 USD) that could be used in a wide variety of stores for their participation. If the participants suffered from any kind of illness, the name of the illness was noted by the study recruiter. All diagnoses were reviewed by a physician from Ichilov Hospital. Of the 1,149 people contacted, 451 (39.3%) chose not to participate, 138 (12.0%) no longer had a person at home who met criteria for inclusion, 53 (4.6%) were on vacation or absent during data collection, and 337 had unavailable numbers (29.3%). This resulted in 170 individuals (14.8%) who agreed to participate in the study. Participants were interviewed in their homes where informed consent was obtained and blood spot samples were collected on filter paper using a standard procedure (McDade, Burhop, & Dohnal, 2004). The finger was cleaned with an isopropyl alcohol pad, pricked with a sterile, disposable microlancet (Microtainer, Franklin Lakes, NJ) and five drops of blood (~50 uL/drop) were absorbed onto standardized filter paper (Schleicher and Schuell #903, Keene, NH). The blood spots were air dried and stored in low gas-permeable zip-closure bags. Blood spots were shipped on dry ice and analyzed at Rush University Medical Center. Participants' body weight was measured using portable mechanical scales that were calibrated and checked before the start of the study and height and waist circumference were measured with measurement tapes, allowing for calculation of body mass index (BMI).

Of the 170 participants, 78 were excluded due to confounds known to impact immune functioning including infection in the past 2 weeks, current aspirin use, current statin use,

Table 1
Participant Demographics

Variable	High-terror exposure		Low-terror exposure		Total	
	n	%	*n*	%	*n*	%
Marital status						
Single	15	34.1	9	18.8	24	26.1
Married	29	65.9	39	81.3	68	73.9
Education						
< High school	2	4.5	4	8.4	6	6.5
High school	20	45.5	20	41.7	40	43.4
Some college	7	15.9	9	18.8	16	17.4
College	15	34.1	15	31.3	30	32.6
Income (NIS)						
Below 4,500	7	15.9	1	2.1	8	8.7
4,500–7,500	6	13.6	5	10.4	11	11.9
7,500–10,500	12	27.3	13	27.1	25	27.1
10,500–13,500	12	27.3	14	29.2	26	28.3
Over 13,500	3	6.8	9	18.8	12	13.0
Decline to answer	4	9.1	6	12.5	10	10.9

Note. $N = 92$. NIS = New Israeli shekel.

hypertension, diabetes, and ischemic heart disease. This resulted in 92 participants included in the current study. Of these, 46.7% were male and the mean age was 45.80 years (SD = 12.08). See Table 1 for additional demographics of the final sample. Of the total sample of 92, 44 participants were from the high terror-exposed group, and 48 were from the low terror-exposed group. Mean BMI (27.11, SD = 5.22) indicated an overweight sample on average. Average household monthly income was between 7,500–10,500 NIS (the national average is 9,000 NIS). A comparison of follow-up participants to decliners indicated that there were no significant differences with regard to sex, χ^2 (1, $N = 1{,}149$) = 0.14, $p = .708$, immigration status, $\chi^2(1, N = 1{,}145) = 2.63$, $p = .105$, educational attainment, $t(1131) = -1.64$, $p = .101$, religiosity level, $t(1132) = -.71$, $p = .447$, political orientation, $t(975) = -.65$, $p = .513$, and income level, $t(958) = .07$, $p = .942$. Participants were significantly older ($M = 47.58$ $SD = 14.49$) than decliners ($M = 43.89$ $SD = 43.89$), t (252.61) = 2.96, $p = .003$. Participants were more likely to be married (76.9%) than were decliners (53.8%), χ^2 (1, $N = 1{,}141$) = 9.19, $p = .002$. Among participants, 34.3% reported one trauma exposure, 14.2% reported two trauma exposures, and 4.7% reported three or more trauma exposures. Of decliners, 25.6% reported one trauma exposure, 12.2% reported two trauma exposures, and 3.8% reported three or more trauma exposures. This difference in frequency of trauma exposure between participants and decliners was statistically significant, $\chi^2(1, N = 1{,}138) = 8.31$, $p = .040$.

Measures

The Patient Health Questionnaire-9 (PHQ-9) Depression Scale (Kroenke, Spitzer, & Williams, 2001), a component of the broader Patient Health Questionnaire, is a 9-item measure that assesses depressive symptom severity and has been demonstrated to be highly sensitive in identifying these symptoms. The PHQ-9 has previously been used in Israeli and Palestinian populations (Hobfoll et al., 2008). Participants were asked how frequently they experienced each symptom during the previous 2 weeks ranging from 0 = *not at all* to 3 = *nearly every day*. Internal consistency for the PHQ-9 in these data was $\alpha = .91$. Summed scores were used in predictive models, and meeting criteria for probable depression was determined by endorsement of one of the two core depression criteria (depressed mood or anhedonia) plus at least five other symptoms on the PHQ-9. An item was considered to be endorsed if scored as 2 = *more than half the days* or 3 = *nearly every day*.

The PTSD Symptom Scale-Self Report (PSS-SR; Foa, Riggs, Dancu, & Rothbaum, 1993) is a 17-item measure that assesses participants' symptoms associated with PTSD. Participants are instructed to indicate the extent to which they have been distressed by each symptom in the past month, as related to political violence event(s) they experienced, on a scale from 0 = *not at all* to 3 = *very much*. Specifically, participants responded to their reactions to "rocket attacks (missiles and mortars) and terror attacks." This measure was worded the same for both high-exposure and low-exposure groups, as some participants in the low-exposure group may have been personally exposed to terror. This measure has demonstrated adequate psychometric properties when used previously with Palestinian and Jewish samples (Hall et al., 2008; Hobfoll, Canetti-Nisim, & Johnson, 2006; Hobfoll et al., 2008; Palmieri, Canetti-Nisim, Galea, Johnson, & Hobfoll, 2008). The PSS-SR had an internal consistency of $\alpha = .93$. Probable diagnosis of PTSD was established by using the *Diagnostic and Statistical Manual for Mental Disorders* (4th ed.; *DSM-IV*; American Psychiatric Association, 2000) PTSD criteria, with endorsement of a 1 = *once per week/a little bit* considered endorsement of the symptom. Statistical models were based on summed scores for total PTSD and for reexperiencing, avoidance/numbing, and hyperarousal.

Immunoassays for CRP and antibodies to CMV samples were extracted from a 3.1-mm disk punched from each blood spot sample and eluted overnight at 8°C in 250 μl of appropriate assay diluents supplied with the kit for CMV or phosphate buffered saline (PBS) for CRP. These methods have been well validated in previous studies. For instance, CRP measured in blood spots and from blood samples taken by venipuncture was highly correlated and blood spot CRP was stable at room temperature (McDade et al., 2004). CMV antibody measurement from blood spots was similarly validated in previous studies (Dowd, Aiello, Chyu, Huang, & McDade, 2011). The validation reported by others was reconfirmed in this laboratory; CRP or CMV antibodies were highly correlated between plasma samples collected traditionally using venipuncture and

in blood spots from the same individuals (CRP: $r = .98$; $p < .001$; $n = 8$; and CMV antibodies: $r = .99$, $p < .001$, $n = 18$). Blood was collected into citrated tubes by a trained phlebotomist. The blood was spotted directly on the paper disk or an aliquot was centrifuged (1,000 g) to obtain plasma that was frozen (−80°C) until use. The CRP and CMV antibodies were measured in paired samples and the correlation coefficient and significance determined. These blood spot collection methods have also been utilized in recent research on PTSD and CRP (Heath et al., 2013).

CMV assays were performed according to the manufacturer's protocol (*Is*-CMV IgG Test Kit, Diamedix Corporation, Miami, FL). Briefly, 100 μl of the solution extracted from the disk (equivalent to 1:100 dilution of serum), diluted control and calibration sera were added to wells in duplicate and incubated (1 hr, 37°C). The plates were washed with wash buffer and incubated with 100 μl of diluted enzyme tracer (1 hr, 37°C). After washing, the wells were incubated with chromogen substrate and the reaction was stopped by adding acid. Plates were read with an ELISA (enzyme-linked immunosorbent assay) reader at 450 nm with 630 nm as a reference. Graphs were generated using standard concentration calibrators. If the values obtained for test samples were above the standard range, the extracted sample was further diluted and retested.

CRP was measured using the DRG® CRP HS ELISA (EIA-3954) kit. Calibrators for CRP blood spots were prepared by diluting CRP (standardized against the WHO International Reference Preparation; #X0923, Dako, Carpinteria, CA) with washed erythrocytes for 20 mg/ml, 10 mg/ml, 5 mg/ml, 2.5 mg/ml, 1 mg/ml, 0.5 mg/ml, 0.025 mg/ml, and 0 mg/ml concentration followed by application onto filter paper. The dried blood spots were extracted from the filter paper with 250 μl of PBS containing 0.3% Tween 20 overnight (8°C). Blood spot calibrators, controls, and samples were included in all assays and were treated identically throughout the protocol. Ten μl of the extracted sample, controls and standards were added to duplicate wells. One hundred microliters of enzyme conjugate detection reagent was added (22°C, 45 min). Wells were washed and incubated with chromogen substrate to develop color for 20 minutes and the reaction was stopped by adding acid. Plates were read with an ELISA reader at 450 nm and values were obtained by extrapolation from the standard curve.

Demographic information collected included age, marital status (coded 1 = *single/divorced/separated/widowed*, 2 = *married*), education (1 = *less than high school,* 2 = *high school graduate,* 3 = *some college,* 4 = *college graduate*), and income.

Data Analysis

Descriptive statistics and correlations were calculated to characterize the study variables and their interrelationships. Correlations were used to evaluate the relationships between demographic and anthropometric variables including age and BMI that could be associated with key study variables (Heath et al., 2013). Missing data were managed using list-wise deletion. Hierarchical multiple regression assessed the independent contribution of terror exposure, depression, and PTSD in accounting for CRP levels. Given the multiple components of PTSD, some analyses were repeated with PTSD cluster scores. Given prior paradoxical findings on PTSD, and immune and inflammatory markers (Söndergaard et al., 2004), analyses were also conducted to determine whether the relationships between PTSD and CMV antibodies and CRP levels varied based on participant age similar to a moderation-type framework (Hayes, 2012).

Results

PSS total symptom scores indicated that 20.2% of the sample met *DSM-IV* criteria for probable PTSD, and the PHQ-9 indicated 7.7% met criteria for probable depression.

Correlations between demographic and anthropometric variables, the PSS and PHQ-9 symptom scores, and CMV antibodies and CRP were examined (see Table 2). BMI was not significantly related to trauma exposure, PSS-SR scores, or PHQ-9 scores. BMI was significantly correlated with both CMV antibodies, $r = .32$, $p = .004$, and CRP, $r = .41$, $p < .001$, and was included in regression models to assess its relative relationship to CRP. Age was significantly associated with CMV antibodies, $r = .22$, $p = .049$, but not with CRP. Sex and education were not significantly associated with either CMV antibodies or CRP. Smoking data were available for some of the samples in the recruitment pool for this study. For this group ($n = 60$), smoking was unrelated to CRP or CMV.

CRP was significantly correlated with total PSS-SR score, and PSS-SR scores for PTSD Criterion B (reexperiencing), and Criterion C (avoidance). CRP and PHQ-9 depression were not significantly associated. To test the first hypothesis, that higher PSS total symptom scores would be significantly associated with elevated CRP levels after including BMI, exposure to terror, and depression in the model, hierarchical linear regression was used to regress CRP values on PSS-SR scores (Table 3). BMI was included as a first step in these analyses, as it was significantly associated with CRP. To examine the possibility that any significant effect might be due to exposure to terror or depression symptoms, and not PTSD, these variables were then entered in the model in separate steps. PSS total symptom score was included as the final step.

As can be seen in Table 3, the PSS total symptom score remained significant, $\beta = .33$, $p = .034$, when including BMI, depression, and exposure to terrorism. Follow-up analysis indicated that the association between PSS total symptom score and CRP remained significant when age was added to the model, $\beta = .34$, $p = .031$. Age did not moderate the relationship between PTSD and CMV antibodies (interaction $p = .753$), nor the relationship between PTSD and CRP (interaction $p = .895$). Next, we replaced the PSS total score with PSS scores for Criterion B, C, and D in three separate additional regressions. Given the significant correlations between CRP and Criteria B and C, we expected these also to be significant predictors of CRP values in

Table 2
Descriptive Statistics and Zero-Order Correlations Between All Study Variables

Variable	*M*	*SD*	1.	2.	3.	4.	5.	6.	7.	8.	9.
1.Age	45.80	12.08	—								
2. BMI	27.11	5.22	.12	—							
3.Exposure	0.86	0.99	−.07	.07	—						
4.PHQ-9	12.90	4.69	−.03	−.01	.09	—					
5.PSS Total	8.07	9.06	.10	.06	.31**	.67**	—				
6.PSS B	2.57	3.34	.08	.15	.40**	.52**	.91**	—			
7.PSS C	2.52	3.23	.03	.01	.28**	.60**	.92**	.76**	—		
8.PSS D	2.98	3.32	.16	.00	.17	.75**	.92**	.75**	.77**	—	
9. CMV	116.71	90.00	.22*	.32**	−.13	.20	.17	.21	.06	.20*	—
10.CRP	2.77	4.68	.03	.41**	.04	.12	.27*	.29**	.27*	.18	.23*

Note. $N = 92$. Missing data were removed from analyses using list-wise deletion. BMI = body mass index; PHQ-9 = Patient Health Questionnaire-9—Depression; PSS = PTSD Symptom Scale-Self Report; PSS B = PTSD Criterion B; PSS C = PTSD Criterion C; PSS D = PTSD Criterion D; CMV = antibodies to cytomegalovirus; CRP = C-reactive protein.
*$p < .05$. **$p < .01$.

regression analyses and Criterion D to be a nonsignificant predictor. As expected, Criterion B, $\beta = .27$, $p = .053$, and C, $\beta = .31$, $p = .021$, remained significant, whereas Criterion D, $\beta = .16$, $p = .327$, was not. Thus, CRP may be more strongly associated with intrusive and avoidant/numbing symptoms of PTSD than with hyperarousal.

CMV antibodies were not significantly associated with PHQ-9 depression total score, $r = .20$, $p = .075$, or PSS total score, $r = .17$, $p = .127$. There were no significant associations between CMV antibodies and PTSD Criterion B (re-experiencing), r = .21, $p = .070$; Criterion C (avoidance), $r = .06$, $p = .576$; or Criterion D (hyperarousal), $r = .21$, $p = .073$. Given the nonsignificant associations between depression and PTSD, multivariate models were not explored.

Table 3
Regression Models of C-Reactive Protein on PSS Total Scores

Variable	Model	B	*SE*	β	*t*	R^2	ΔR^2
	1					.17	.17**
BMI		0.36	0.09	.41	.93**		
	2					.17	—
BMI		0.36	0.09	.41	3.92**		
Terror exposure		0.21	0.49	.05	.42		
	3					.19	.02
BMI		0.37	0.09	.42	.98**		
Terror exposure		0.11	0.49	.02	.23		
PHQ-9		0.14	0.11	.13	.24		
	4					.24	.05*
BMI		0.34	0.09	.39	.78**		
Terror exposure		−0.28	0.51	−.06	−.54		
PHQ-9		−0.09	0.15	−.08	−.58		
PSS total		2.88	1.33	.33	2.16*		

Note. Final $n = 77$ after list-wise deletion of missing data. BMI = body mass index; PHQ-9 = Patient Health Questionnaire-9; PSS = PTSD Symptom Scale-Self Report.
*$p < .05$. **$p < .01$.

Discussion

The results lend support for the hypothesis that war and terrorism-associated PTSD may lead to immune system dysregulation (elevating levels of CRP). The hierarchical linear regression analysis further suggests that the differences in CRP are brought about by intrusive and avoidant symptoms, but not hyperarousal. This is consistent with previous research conducted mainly on military veterans (Miller et al., 2001; von Känel et al., 2007). We found no association between symptoms of depression and CRP. After including potential confounding variables, overall PTSD symptoms accounted for a statistically significant 5% of the variance in CRP. Depression and PTSD Criterions B and C did not show statistically significant relationships with CMV.

Caution is required in interpreting our results. We relied on a small sample, cross-sectional design, and self-report data. The small sample precluded case-control designs that afford comparisons of immune function among participants with and without PTSD diagnoses. We investigated continuous relationships between PTSD symptoms and immune dysregulation. The small sample also precluded analysis of health variables including sleep, smoking, medication adherence, exercise, chronic diseases, and self-medicating behavior that might mediate the impact of PTSD and depression symptoms on immune dysregulation. By examining both PTSD and depression symptoms, we can to some extent separate their respective influences, but larger samples would also be required to distinguish between the influences of PTSD, which often contains elements of depression, and those of depression that is not comorbid with PTSD. Although we often refer to those having PTSD and

depression as having comorbidity, however, the two disorders are so overlapping as to cause many to consider them part of a single constellation in many instances (Elhai et al., 2011; Gros, Price, Magruder, & Frueh, 2012).

Given cross-sectional data, the duration of PTSD symptoms was unclear, and length of a disorder may be a key factor in altering immune regulatory processes. We also cannot conclude that PTSD causes inflammation, as a dual susceptibility process is possible. In addition, although participants rated their PTSD symptoms in relation to terrorism and rocket attacks, exposure to prior trauma may kindle increased sensitivity to later trauma (Post, Weiss, Smith, & McCann, 1997). Therefore, some participants may have been more sensitive to terrorism and rocket attacks because they had experienced traumatic events other than or prior to those captured in the current study. Studies utilizing additional stressor information and longitudinal data are needed to describe the interaction between trauma exposure, development of symptoms of PTSD, and inflammation over time. The high percentage of decliners is a weakness as we cannot be sure whether some hidden selection factor influenced our findings, especially as avoidance is an aspect of PTSD itself. Finally, this is one sample of an Israeli population exposed to ongoing terrorism. Studies among different populations are needed to generalize the results to other war-related threats and large-scale natural disasters (Goenjian et al., 2003).

Notwithstanding these concerns, the context from which this sample was drawn is also a study strength. Citizens in countries around the world live in conflict zones, experiencing ongoing or severe episodic threat and exposure to violent conflict. Rigorous empirical research, however, on and in conflict zones that explores the effects of such chronic or severe episodic conflict on civilians' well-being is rare. This study utilizes the Israeli–Palestinian conflict as a natural environment to study the role of PTSD and depression symptoms on immune dysregulation. In so doing, this work addresses an important gap in our understanding of civilians' well-being in conflict zones.

The results contribute to a growing body of literature describing the mechanisms by which exposure to violence triggers psychological distress (Canetti, Hall et al., 2013). The current study also adds to a limited set of studies that examine psychoneuroimmunology in a region of conflict. It is important to understand the effect of cumulative stress and trauma on inflammation in this population given the high exposure both to the chronic stress of the threat of attack and to actual attacks that occur frequently.

The current study has ramifications for policy makers and health professionals who intend to assist individuals living in conflict zones. Effective psychotherapy for patients with PTSD may not only improve their psychological functioning, but potentially improve their long-term physical health as well. Decreasing the amount of inflammation in these patients could potentially decrease their risk for chronic illnesses, including heart disease and cancer (Cohen et al., 2009; Cohen, Marmar, & Neylan, et al., 2009; Gouin, 2011; Steptoe, Hamer, & Chida, 2007). Such a dual impact would also increase the cost effectiveness of psychotherapy (Lazar, 2010).

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