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Attachment orientations and loss adjustment among bereaved spouses

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ABSTRACT

Stressful life events such as losing a spouse can enhance inflammation. Responses to loss may depend, in part, on individual differences in attachment anxiety and avoidance. An individual's attachment orientation (i.e., an individual's levels of attachment anxiety and avoidance) reflects how an individual relates to others– specifically, whether they feel their trusted others will reliably be there for them, and whether they feel comfortable opening up to and depending on their relationship partners. This study investigated the association between attachment orientations and poor loss adjustment in recently bereaved individuals (N = 100). Poor loss adjustment was operationalized as greater levels of inflammation and grief symptoms, as well as poorer self-reported mental and physical health. Attachment anxiety was associated with increased stimulated monocyte IL-6 and CCL4 production, but not TNFα. Likewise, attachment anxiety was associated with greater grief symptoms as well as poorer mental and physical health. In contrast, attachment avoidance was not associated with inflammation; it was, however, associated with *less* grief symptoms as well as *better* self-reported mental and physical health. Our findings provide evidence that attachment orientations may be associated with loss adjustment and adverse health outcomes following the recent loss of a spouse.

1. Introduction

The loss of a spouse is a highly stressful event (Stahl et al., 2016). The surviving spouse often endures a range of mental and physical health problems following the loss (e.g.,Kristensen et al., 2012). Hence, bereaved individuals are at an increased risk for morbidity and mortality (Stroebe et al., 2007). Many of the common causes of death among bereaved spouses are thought to be driven by inflammatory-related sequelae such as cardiovascular disease, coronary heart disease, stroke, and cancer (Grivennikov et al., 2010; Hart et al., 2007; Kaptoge et al., 2014). Indeed, recently bereaved individuals exhibit increased levels of circulating pro-inflammatory cytokines (Cohen et al., 2015; Fagundes et al., 2018; Schultze-Florey et al., 2012). Thus, it is important to understand what factors influence loss adjustment, especially inflammation, during bereavement.

Individual differences in responses to loss may depend, in part, on one's attachment orientation (Bowlby, 1980). An attachment figure is an important person in one's life whom an individual turns to in times of need, and seeks for support and emotional security (Trinke and Bartholomew, 1997). Adults most commonly identify their long-term romantic partners as primary attachment figures (Hazan and Zeifman, 1999). Individuals with secure attachment typically have a history of responsive attachment figures, who have reliably been able to comfort them in times of stress. In contrast, those with a history of inconsistent and/or unresponsive attachment figures, develop other strategies to regulate their emotions characterized by anxiety and avoidance (Cassidy and Shaver, 2002). Individuals develop a pattern of expectations over time about whether trusted others will reliably be there for them, and whether they feel comfortable opening up to and depending on their relationship partners. Internal "working models" of attachment guide future behavior in close relationships throughout the lifespan.

The two orthogonal dimensions of attachment anxiety and avoidance reflect the degree to which an individual utilizes anxious and/or avoidance strategies (Shaver and Mikulincer, 2007). People high in attachment anxiety are preoccupied with their partner's accessibility and excessively worry about rejection and abandonment (Brennan et al., 1998); in this way, attachment anxiety can also be thought of as a chronic interpersonal stressor (Fagundes et al., 2014; Powers et al., 2006). An individual high in attachment avoidance is uncomfortable with closeness, emotionally distances themselves from others, and prefers to remain highly independent and self-sufficient (Fraley and Shaver, 2000). Where an individual falls on these dimensions tends to remain relatively stable (Shaver and Mikulincer, 2007).

A number of theorists have posited that individuals high in attachment anxiety, and some cases attachment avoidance, are at a higher risk for developing complications in the grieving process (e.g.,

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Bonanno et al., 2002; Bowlby, 1980; Carr et al., 2000) proposed that Complicated Grief (CG), a condition involving a persistent yearning/longing for the deceased, preoccupation with the deceased, difficulty accepting the loss, and a number of distressing symptoms, is characterized by attachment anxiety; the definition of attachment anxiety includes a tendency to respond to loss with anxious clinging-type responses (Bowlby, 1980). Hence, it is not surprising that individuals high in attachment anxiety exhibit poor loss outcomes compared to their less anxious counterparts (Field and Sundin, 2001; Fraley and Bonanno, 2004; Waskowic and Chartier, 2003; Wayment and Vierthaler, 2002). Indeed, there is a consistent significant positive relationship between attachment anxiety and grief symptoms, but conflicting evidence for attachment avoidance (e.g., Fraley and Bonanno, 2004; Meier et al., 2013). For example, attachment orientations accounted for differences in prolonged grief symptoms beyond demographic factors, and loss-related variables (i.e., cause of death, relationship to the deceased). Specifically, attachment anxiety was uniquely related to prolonged grief symptoms, whereas attachment avoidance was not (Meier et al., 2013).

To our knowledge, researchers have yet to identify whether attachment anxiety and attachment avoidance is related to inflammation after losing a spouse. The sparse literature on attachment orientations and inflammation in other relationship contexts report conflicting evidence. For example, relationship-specific attachment styles were not independent predictors of inflammation (i.e., levels of Interleukin-6 (IL-6), fibrinogen, & C-Reactive Protein (CRP)) among individuals currently in a relationship (Uchino et al., 2013). Attachment avoidance did, however, predict inflammatory responses, evidenced by increased production of IL-6, in other stressful relationship contexts (e.g., during marital conflicts; Gouin et al., 2009). It is still unknown, however, whether attachment orientations in adulthood are associated with inflammation after a relationship loss.

This study is significant in that it utilizes attachment theory, a well-established theoretical framework, to understand individual differences in loss adjustment following the recent loss of a spouse. We hypothesized that attachment anxiety would be associated with poorer loss adjustment operationalized by elevated levels of inflammation, grief symptoms, and poorer self-reported mental and physical health. Given the discrepancies in the literature between attachment avoidance and loss adjustment, it is unclear whether individuals high in attachment avoidance would also exhibit an elevated pro-inflammatory state, grief symptoms, and worse self-reported mental and physical health. Thus, we will treat the anxious attachment hypotheses as exploratory.

Circulating levels of cytokines are affected by a range of factors, and may fall below the threshold of detection, or display significant variation on relatively small-time scales (Steptoe et al., 2007). Consequently, we chose to analyze the capacity of blood mononuclear cells to produce inflammatory mediators after ex vivo stimulation (Korenromp et al., 2011). Utilizing ex vivo stimulation of immune cells offers greater clinical relevance to our findings, as these functional assays better reflect the functional activity of the peripheral immune system, thus providing a powerful evaluation of whole-body inflammation, compared to more crude measures such as circulating cytokine levels.

2. Methods

2.1. Study sample

Individuals who recently experienced the loss of their spouse were contacted and recruited from obituaries, support groups, flyer distribution, online postings, and community events. Exclusion criteria included significant visual or auditory impairment, being pregnant or nursing (women), autoimmune and inflammatory diseases, having experienced bereavement due to the loss of another loved one in the last year, divorced within the past year, and previously widowed. All participants were English-speakers to ensure understanding of the questionnaires. They must have been married to their partner for at least 3 years before the loss. One hundred bereaved participants who had recently lost their spouse, no more than 14 weeks before the visit, participated in the study.

Trained research assistants administered assessments at the participants' home or in the Bioscience Research Collaborative Community Research Center in the Texas Medical Center. During these visits, participants completed a questionnaire packet, including demographic and clinical questionnaires. Anthropometric measurements, including weight, height, and waist circumference and non-fasting blood samples were collected during the early hours of the morning. All samples were collected between 7:30 and 11:00 AM to control for diurnal variation; we also collected data early in the day to limit variability in activity, diet, and stress experienced in the hours before the visit.

The day before the visit, a research assistant called the participants and reminded them of the next day's visit. Given that inflammatory markers may be elevated during acute illnesses (e.g., upper respiratory infections), we asked them if they were experiencing any illness symptoms (e.g., fever, congestion, sore throat, or acute infections due to injury). Participants were asked to avoid any strenuous physical activity 48 hours before all visits. Participants were rescheduled for a different time if they were ill or did not follow the exercise restriction. All participants provided informed consent and procedures were approved by the Rice University Institutional Review Board (IRB).

2.2. Measures

2.2.1. Experiences in close relationships – relationship structures questionnaires (ECR-RS)

To measure attachment anxiety and avoidance, we administered the Experiences in Close Relationships – Relationship Structures Questionnaire (ECR-RS). Participants answered a series of questions about their close relationships in general on a scale of 1 *(Strongly Disagree)* to 7 *(Strongly Agree)* (Fraley et al., 2011). Items include those indicative of attachment anxiety (e.g., *"I'm afraid other people will abandon me,"*) and attachment avoidance (e.g., *"I prefer not to show others how I feel deep down,"*). Anxiety and avoidance mean scores were computed, respectively; scores represent global attachment orientations. The ECR-RS has excellent divergent and convergent validity, as well as an improved predictive value relative to other multi-item attachment scales (Fraley et al., 2011). Cronbach's alpha in the current sample was excellent (Attachment Anxiety, $\alpha = .89$; Attachment Avoidance, $\alpha = .83$). Attachment anxiety and avoidance were used as key independent variables of interest in the current multiple regression analyses.

2.2.2. Cytokines

To measure the reactivity of the monocytes to challenge we treated whole blood to induce cytokine/chemokine production. Specifically, we targeted IL-6, TNFα, and CCL4 ($\alpha = .94$), as these pro-inflammatory monocyte-derived cytokines were elevated in bereaved individuals compared to healthy age-matched controls (Fagundes et al., 2018). Further, IL-6 has an evidenced association with attachment in other stressful contexts (e.g., attachment avoidance predicts inflammatory responses in marital conflicts; Gouin et al., 2009), as well as with bereavement more generally (Schultze-Florey et al., 2012). Elevated TNFα has been associated previously with distress, and is hypothesized to play a role in processing traumatic emotional events (Bruenig et al., 2014). Based on previous research identifying a connection between depression and elevated levels of chemokines in patients with a chronic illness (e.g., Pawlowski et al., 2014), we had reason to believe that a psychosocial factor such as attachment orientation may be associated with elevated chemokines including CCL4 and mental health in the current sample. Supernatants were collected after 24 hours of culture and stored at −80 °C until they were analyzed using multiplex assays according to the manufacturer's instructions (R&D Biosystems). Lipopolysaccharide (LPS)-induced cytokine/chemokine production was

evaluated by heparinized whole blood, diluted 1:10 with RPMI-1640 (Gibco), and was stimulated with 1 ng/ml LPS (Sigma) at 37 ˚C and 5% CO2 for 24 hours. Mean intra- and inter-assay CV (%) values for the different cytokines are as follows: IL-6: intra-assay: 7.4 %; TNF-a: intra-assay: 2%. Pro-inflammatory cytokines were used as dependent variable(s) in the present analyses.

2.2.3. Grief

The Inventory of Complicated Grief was used to measure the degree to which participants experience grief symptoms by answering 19 items on a frequency scale of 0 *(never)* to 4 *(always)* (Prigerson et al., 1999). Example items include, "I feel dazed or stunned over what happened," and, "I hear the voice of the person who died speak to me." This measure was designed and validated as a tool to help practitioners distinguish diagnoses of complicated grief from other bereavement-related emotional disorders such as depression, among those who had lost a spouse (Prigerson et al., 1995). Items were mean scored (α = .92), with higher scores indicating higher grief symptoms.

2.2.4. Mental and physical health

The Medical Outcomes Study RAND SF-36 was implemented as a self-report measure of mental and physical health (Brazier et al., 1992), and contains 8 subscales. These 8 subscales were used to calculate scores for the summary measures of mental and physical health, by calculating a mean across the four subscales mapping onto physical health (i.e., physical functioning, role limitations due to physical health, pain, & general health; α = .78), and a mean across the four subscales mapping onto mental health (i.e., energy/fatigue, social functioning, role limitations due to emotional health, & emotional well-being; α = .78), respectively (Ware, 1993).

2.2.5. Sleep disturbance

The Pittsburgh Sleep Quality Index (PSQI) was used as a measure of sleep disturbance. The PSQI is a widely used instrument for the evaluation of sleep quality across seven areas (subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction) that are aggregated in a global score ranging from 0 to 21 (Buysse et al., 1989). Higher scores on the global score are indicative of greater sleep-related disturbances. A sum of 5 or greater indicates a "poor" sleeper (Smyth, 2003). Participants' PSGI global score was used as a covariate in the current analyses.

2.2.6. The Charlson index

The Charlson Index (Charlson et al., 1994), the most widely used comorbidity index for predicting mortality, was used to assess medical comorbidities. The measure assigns weights to 19 comorbid medical conditions based on their potential influence on one-year mortality. This was used as a covariate in the analyses.

2.2.7. The community healthy activities model program for seniors (CHAMPS)

This questionnaire assessed the weekly frequency and duration of various physical activities. Excellent for middle-aged and older populations (Demark-Wahnefried et al., 2003), we used the moderate exercise index, as defined by the CHAMPS, as a covariate in our analyses.

2.2.8. Center for epidemiologic studies depression scale (CES-D)

The Center for Epidemiologic Studies Depression Scale (CES-D; Radloff, 1977) was used to assess the prevalence of depressive symptoms. This 20 item self-report measure asks participants to indicate whether and how frequently they have experienced depressive symptoms in the past week—for example, "I felt that I could not shake off the blues, even with the help of my family or friends," and "I talked less than usual." Each answer option holds a particular value (from 0 to 3); we calculated a sum total score to use as a dependent variable in ancillary analyses, with higher numbers reflecting more frequent occurrence of depressive symptoms, and lower numbers reflecting less frequent occurrence (α = .92).

2.2.9. Symptom checklist 90

We used the Symptom Checklist 90 (SCL-90-R; Derogatis, 1994) to assess current anxiety symptoms. The SCL-90-R is a self-report measure for a broad range of psychological problems. Participants rate each item on a 5-point scale of distress (0–4), ranging from "Not at all" to "Extremely." Here, we utilize the anxiety subscale (α = .86), which includes 10 items to assess general signs of anxiety (e.g., "feeling fearful" or "nervousness or shakiness inside"). Scores were derived by summing the values for each item response within the anxiety subscale and then dividing by the number of items each participant endorsed. Higher scores indicate greater symptom severity.

2.2.10. Demographics & covariates

Participants provided self-reports of their age, gender, race/ethnicity and education, smoking status, and alcohol use. Body mass index (BMI) was computed as weight in kilograms divided by height in meters squared. We also assessed whether they were taking statins, as this type of medication tends to influence inflammatory processes (Jain and Ridker, 2005). Lastly, participants reported the date of their spouse's passing, which we used to calculate a time since passing variable that represented the number of days between the spouse's date of death and the participant's date of participation in the study.

2.3. Statistical analysis

Preliminary statistical analyses included descriptive statistics and assessment of normality of distributions. We checked the scores to ensure they were biologically possible. We also examined for skewness and kurtosis. The inflammatory markers were skewed, as would be expected. Accordingly, the inflammatory biomarker variables were natural log-transformed to approximate to a normal distribution. After running each analysis, we examined the residuals to ensure that transforming the data improved the distribution. It was determined there were no meaningful outliers, which were quantitatively defined as more than three interquartile ranges from the hinges of a standard boxplot (Howell, 2012). The pro-inflammatory monocyte-derived markers included IL-6 (M = 6.43 pg/mL., SD = 1.48), TNFα (M = 5.09 pg/mL, SD = 1.46), and CCL4 (M = 8.02 pg/mL, SD = .97). TNFα was associated with IL-6 (r = .91, p < .001), and CCL4 (r = 0.88, p < .001). IL-6 was also associated with CCL4 (r = 0.88, p < .001). To reduce type I error, Z scores of these log-transformed inflammatory markers in each participant were averaged to create a pro-inflammatory composite index. These pro-inflammatory markers operate together in vivo; this combined index reflects a coordinated pro-inflammatory immune response. This is a well-established method to analyze multiple correlated dependent variables and has been previously used to examine individual immune markers that function similarly (e.g., Dattalo, 2013). Subsequently, we conducted ancillary analyses on each individual biomarker in separate linear regression models.

Multiple imputation using fully conditional specification (FCS) was employed to impute missing data (which was less than 5% of the sample and did not include any immune data). Multiple imputation produces unbiased parameter estimates that appropriately reflect the true variability of the missing data and has been shown through simulation studies to be a more valid and less biased analytical approach than listwise deletion (Horton and Lipsitz, 2001). The fully conditional specification approach to multiple imputation is flexible in that it does not rely on normality assumptions (Raghunathan et al., 2001) and preserves power (Liu and De, 2015). Following standard practice, the imputation procedure was repeated five times in order to approximate the true measurement variance represented in real data. All analyses

were completed with each of the full imputed data sets, and the coefficients generated by each separate data set were averaged to produce final estimates (Graham, 2009).

We ran four regression models as our primary set of analyses, all of which included attachment anxiety and avoidance as primary independent variables of interest. In the first model, the pro-inflammatory composite was the dependent variable. In the second model, grief symptoms was the dependent variable. In the third model, self-reported mental health was the dependent variable, and in the fourth, self-reported physical health. We decomposed the pro-inflammatory composite in secondary analyses, to investigate effects on the individual pro-inflammatory biomarkers (IL-6, TNFα, CCL4). All analyses were run using multiple regression in SPSS. For models with proinflammatory outcomes, we adjusted for age, sex, BMI, physical activity, comorbidities, sleep disturbance, alcohol use, statin use, and days since spouse's passing. Smoking status (1 = current smoker, 0 = nonsmoker) was coded as a categorical variable. For the models with the self-reported health outcomes, we maintained the covariates from the inflammatory analyses that were theoretically significant and/or if they exhibited a significant correlation with one or more of our self-reported outcomes: grief symptoms, mental health, and physical health. These covariates were sleep quality, BMI, age, alcohol use, time since passing, and smoking status.

We were careful not to adjust for extraneous factors to reduce risk of overfitting the models. For example, we did not exclude or adjust for aspirin use because 325 mg/day did not reduce IL-6 and CRP inflammation in a prospective cross-over design with 37 healthy volunteers (Azar et al., 2003). Further, an epidemiological study found that individuals taking antidepressants did not have significantly lower levels on key markers of inflammation than individuals who are not taking antidepressants (Penninx et al., 2003). Thus, we elected not to adjust for anti-depressants.

3. Results

Study sample characteristics are presented in Table 1. Bivariate correlations (see Table 2) revealed that attachment anxiety was associated with attachment avoidance (as expected), IL-6, and CCL-4 (*ps* < .05), while attachment avoidance was not significantly associated with any of the other variables of interest (*p* = ns). We hypothesized that attachment anxiety would be associated with the pro-inflammatory composite, even when including attachment avoidance and the proposed covariates in the model. Because attachment avoidance and attachment anxiety comprise two theoretically orthogonal dimensions of attachment orientation, we included both variables in the regression equation, as is standard in attachment research (e.g., Fagundes et al., 2014). We found that attachment anxiety, but not attachment avoidance, was associated with the pro-inflammatory composite (see Table 3), such that those higher in attachment anxiety also had higher levels of inflammation compared to those who reported lower attachment anxiety. We then conducted post-hoc tests to evaluate each individual inflammatory marker (natural logged). When including the covariates in the model, attachment anxiety was associated with monocyte stimulated IL-6 ($b = .09$, $p = .03$, $sr^2 = 0.23$) and CCL4 ($b = 0.06$, $p = .04$, $sr^2 = .22$), but not TNFα ($b = 0.06$, $p = .14$, $sr^2 = 0.15$). In the same pattern as the pro-inflammatory composite, attachment avoidance was not associated with any of the individual pro-inflammatory biomarkers (IL-6, $b = -0.02$, $p = .38$, $sr^2 = -.09$; CCL4, $b = -0.02$, $p = .25$, $sr^2 = -.12$; TNFα, $b = -0.03$, $p = .24$, $sr^2 = -.12$). Likewise, higher levels of attachment anxiety was associated with more grief symptoms and better mental and physical health, compared to lower levels of attachment anxiety. Although attachment avoidance was not significantly associated with circulating levels of inflammation (as reported above), participants high in avoidance reported significantly fewer grief symptoms, as well as better mental and physical health compared to those low in avoidance (see Table 4).

Table 1
Study Sample Characteristics.

Variable	Number (%) or mean (SD)
Age	68.64 (10.65)
Sex	
Male	28 (28.0)
Female	72 (72.0)
Race	
White	89 (89.0)
Black or African American	4 (4.0)
Asian	2 (2.0)
Other	5 (5.0)
Ethnicity	
Hispanic/Latinx	10 (10.0)
Not Hispanic/Latinx	85 (85.0)
Not applicable	5 (5.0)
Education	
College degree or higher (Bachelor's, Master's, PhD, MD, or other higher degree)	59 (59.0)
≥ 3 years of college	18 (18.0)
< 3 years of college	10 (10.0)
High school graduate	10 (10.0)
< High school	2 (2.0)
not applicable	1 (1.0)
Yes	5 (5.0)
No	95 (95.0)
Statins	
No	59 (59.0)
Yes	41 (41.0)
Attachment anxiety	7.17 (4.39)
Attachment avoidance	17.91 (7.15)
Il-6†	6.43 (1.48)
TNF- -α†	5.09 (1.46)
CCl4†	8.02 (.91)
Proinflammatory composite†	.00 (.96)
Grief Symptoms	21.67 (12.14)
Mental health	62.27 (21.32)
Physical health	75.71 (19.8)
Comorbidities	.24 (.93)
Sleep disturbance	7.36 (6.15)
Physical activity	2866.38 (3889.10)
BMI	26.94 (4.89)
Alcohol use	3.82 (5.32)
Smoking status	.95 (.22)
Time since passing	84.74 (18.17)
Statins	.41 (.49)

† natural logarithm transformed.

In an ancillary analysis using the same covariates noted above for analyses with self-reported outcomes, we found that attachment anxiety ($b = .93$, $p < .001$), but not attachment avoidance ($b = -0.22$, $p = .15$), was significantly associated with depressive symptoms, as indicated by the Center for Epidemiologic Studies Depression Scale (CES-D; Radloff, 1977); those high in attachment anxiety reported more depressive symptoms than those lower in attachment anxiety. To rule out the possibility that the relationship between attachment anxiety and inflammation merely reflects a relationship between social anxiety and inflammation more generally, we tested social anxiety as an independent variable in our model. In a model using the same covariates as those used in our primary inflammatory analysis, we found that anxiety, as indexed by the Symptom Checklist 90 (SCL-90; Derogatis, 1994), was not significantly associated with the inflammatory composite ($b = -0.03$, $p = .325$). We also tested for the attachment anxiety × attachment avoidance interaction and it was not significant ($b = -.001$, $p = .239$). Further, using Hayes (2017) approach, we investigated whether mental health, physical health, or perceived stress (respectively) statistically mediated the relationship between attachment anxiety and the proinflammatory composite; we found no significant indirect effects (defined by confidence intervals that included 0).

Table 2
Bivariate correlations (Spearman's Rho) between variables of interest.

Variable	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18
1. Anxious attachment	–																	
2. Avoidant attachment	.53***	–																
3. IL-6†	.22*	.04	–															
4. TNF-α†	.15	-.09	.91***	–														
5. CCL4†	.22*	-.01	.84***	.84***	–													
6. Proinflammatory composite†	.19	-.03	.95***	.95***	.94***	–												
7. Mental health	-.19	.05	.09	.10	.04	.07	–											
8. Physical health	-.15	.03	-.02	.01	-.08	-.03	.50***	–										
9. Comorbidities	-.05	-.02	.01	.02	-.01	-.01	.11	-.15	–									
10. Sleep quality	.01	.02	-.04	-.05	-.06	-.06	-.40***	-.26*	-.02	–								
11. Physical activity	.04	.05	-.16	-.09	-.07	-.10	.10	.25*	.07	-.43***	–							
12. BMI	.06	.06	-.04	-.04	-.03	-.04	-.22*	-.29**	.19	.13	-.14	–						
13. Age	-.05	.00	.08	.09	.10	.09	.37***	-.10	.19	-.12	.01	-.03	–					
14. Sex	-.10	-.14	.00	-.04	.02	.00	-.28**	-.12	-.14	.08	-.07	-.25*	-.25*	–				
15. Alcohol use	.05	-.07	.05	.06	.04	.05	.08	.18	-.22*	.11	-.04	.05	-.04	-.11	–			
16. Smoking status	.01	.13	.02	-.02	.06	.02	-.18	-.22*	-.08	.10	-.03	.07	-.09	-.06	.06	–		
17. Time since passing	.06	-.19	.22*	.16	.12	.17	.06	.07	-.02	.02	-.15	-.17	.07	.13	.06	-.05	–	
18. Statins	.11	.14	.09	.11	.06	.09	.16	.11	.17	-.08	.08	.05	.31**	-.16	.24*	.00	.00	–

Note. † natural logarithm transformed; Proinflammatory composite reflects the mean of each z scored biomarker (IL-6, TNF- α, CCL4), after natural log transformation;

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

Table 3
Multiple Regression Results Depicting a Proinflammatory Composite as a Function of Variables of Interest.

Variables	*b*	*SE*	*t*	*Sig*	*sr*
Sleep quality	-.02	.02	−1.18	.312	-.12
Comorbidities	-.01	.11	-.06	.904	-.01
Physical activity	.00	.00	−1.72	.129	-.17
BMI	.00	.02	.01	.885	.00
Age	.01	.01	1.08	.293	.11
Sex	.04	.23	.18	.856	.02
Alcohol use	.00	.02	.14	.885	.01
Time since passing	.01	.01	1.27	.207	.13
Statins	-.01	.23	-.05	.803	.00
Smoking status	.41	.47	.88	.389	.09
Attachment anxiety	**.06**	**.03**	**2.05**	**.045***	**.21**
Attachment avoidance	**-.02**	**.02**	**-1.12**	**.269**	**-.11**

Note. Sex coded 0 = Male, 1 = Female; Alcohol use refers to number of drinks per week; Time Since Passing refers to number of days since spouses' death at time of study measurements; Smoking status coded 0 = yes, 1 = no. *$p < .05$.

4. Discussion

This is the first study to investigate whether attachment orientations are related to immune dysregulation among a sample of spousally bereaved individuals. We hypothesized that attachment anxiety would be associated with poorer loss adjustment operationalized by elevated levels of inflammation and grief symptoms, as well as worse mental and physical health. Indeed, we found that attachment anxiety, but not attachment avoidance, was associated with increased stimulated monocyte IL-6 and CCL4 production. Interestingly, neither individuals high in attachment anxiety nor those high in attachment avoidance exhibited higher levels of increased stimulated monocyte TNFα, compared to those who scored lower on these dimensions. Those high in attachment anxiety reported greater grief symptoms, and worse mental and physical health overall, compared to those lower in attachment anxiety. In contrast, those high in attachment avoidance reported *less* grief symptoms, and *better* mental and physical health compared to those low in attachment avoidance. Our findings are consistent with the larger body of attachment research that documents greater distress among individuals with attachment anxiety who experienced the loss of a romantic partner (i.e., breakup, divorce, death of a spouse; Shear and Shair, 2005). In contrast, the aforementioned findings provide evidence that attachment avoidance may be adaptive during the first three months after the loss of a spouse.

The exact mechanisms through which social relationships influence health outcomes remain unclear (Uchino et al., 2012). How an individual appraises stress and one's ability to emotionally regulate following a stressor, may be more predictive of health outcomes than exposure to stressors alone (DeSteno et al., 2013). Individuals high in attachment anxiety typically have not mastered self-regulatory strategies, which leaves them vulnerable to chronically heightened stress reactivity and an inability to down-regulate negative emotions (Shaver and Mikulincer, 2002). Alternatively, individuals high in attachment avoidance strive to suppress the distress caused by failed bids for support from others (Kobak and Sceery, 1988). Future research should

Table 4
Multiple Regression Results Depicting the Relationship Between Attachment Variables & Self-reported Health Outcomes.

	b	*SE*	*t*	*Sig*	*sr*	*b*	*SE*	*t*	*Sig*	*sr*	*b*	*SE*	*t*	*Sig*	*sr*
Sleep quality	.67	.19	3.27	.079	.28	−1.34	.29	−4.42	.005*	-.33	-.71	.29	−2.43	.064	-.19
Body mass index	-.23	.23	−1.00	.351	-.09	-.81	.34	−2.38	.035*	-.18	−1.60	.34	−4.69	.000*	-.38
Age	-.24	.11	−2.28	.03*	-.20	.41	.16	2.61	.014	.20	-.52	.16	−3.29	.002*	-.27
Sex	−1.65	2.56	-.65	.538	-.06	−10.87	3.83	−2.85	.008*	-.21	−9.77	3.81	−2.57	.013*	-.21
Alcohol use	-.28	.21	−1.34	.202	-.12	.70	.31	2.24	.035*	.17	.81	.31	2.59	.011*	.21
Time since passing	-.122	.06	−1.97	.056	-.17	.11	.09	1.20	.249	.09	.06	.09	.60	.554	.05
Smoking status	3.15	5.02	.62	.541	.06	−20.25	7.51	−2.70	.010*	-.20	−20.95	7.48	−2.80	.007*	-.23
Attachment anxiety	**1.04**	**.297**	**3.49**	**.001***	**.31**	**-1.87**	**.44**	**-4.21**	**.000***	**-.32**	**-1.17**	**.44**	**-2.64**	**.010***	**-.21**
Attachment avoidance	**-.42**	**.19**	**-2.22**	**.030***	**-.20**	**.73**	**.28**	**2.61**	**.011***	**.20**	**.57**	**.28**	**2.03**	**.046***	**.16**

Note. Sex coded 0 = Male, 1 = Female; Alcohol use refers to number of drinks per week; Time Since Passing refers to number of days since spouses' death at time of study measurements; Smoking status coded 1 = yes, 0 = no. * $p < .05$.

elucidate the interplay between attachment dimensions and emotion regulation processes in predicting health outcomes.

It is important to keep in mind a few key features of our bereaved sample. The current sample had experienced the loss of a spouse in the last 3 months (M = 84.74 days, SD = 18.17), so our results may only reflect the more immediate impact of grief on loss adjustment. Individuals high in attachment avoidance use deactivating strategies (e.g., denial of attachment needs & minimization of emotional pain) to avoid distress (Mikulincer et al., 2006). It may be the case that using avoidant (i.e., deactivating) strategies to cope with loss may serve as a buffer in the short term but may exacerbate issues in the long term, as these individuals may have delayed fully processing the loss. Fraley and Bonanno (2004) found that avoidance was related to an increase in grief symptoms over the first 18 months after a loss. Perhaps the scope of this study does not fully capture the potentially deleterious effects of avoidant strategies for dealing with bereavement, such as a lack of support seeking and a reluctance to fully process the loss (Mikulincer and Florian, 1995). Further, the context and nature of the loss (e.g., whether it was sudden or expected), as well as the person's relationship with the individual they lost (e.g., spouse, sibling, child), may also have an impact. Longitudinal data are needed to assess inflammatory and self-reported health changes over time among avoidant individuals after different types of relationship loss.

In ancillary analyses, we tested mental health, physical health, and perceived stress (separately) as potential statistical mediators of the relationship between anxious attachment and inflammation, and found no significant mediation. While identifying a mechanistic link between attachment anxiety and inflammation is important, these results should be taken cautiously given the inflated Type I and Type II error rate, which comes with utilizing bootstrapping with such a small sample (MacKinnon et al., 2004). Future research should employ research designs (e.g., longitudinal data collected with a large sample) that better allow for strong tests of statistical mediation. While perceived stress was not a significant mediator using the current sample, given the central pathway by which psychological states promote inflammation is via glucocorticoid resistance (Miller et al., 2002), a chronic state of attachment anxiety, a trait-like individual difference factor, is likely a more stable indicator of chronic low grade inflammation, than current or "state" stress levels.

This study has several strengths. Utilizing ex vivo stimulation of immune cells offers greater clinical relevance to our findings, as these functional assays better reflect the functional activity of the peripheral immune system, compared to more crude measures such as circulating cytokine levels. Second, studying attachment and inflammation in the context of bereavement is an important contribution to the literature, as the impact of attachment orientations may operate differently in the context of relationship loss compared to other relationship-related stressors. Gouin and colleagues (2009) found that those high in attachment avoidance had higher IL-6 production during marital conflict in the laboratory compared to those with lower attachment avoidance, perhaps underscoring the context-dependent utility of avoidant emotion regulation strategies. Therefore, Gouin and colleagues' (2009) findings may not reflect how individuals high in avoidant attachment may respond to the loss of their marital partner altogether. Moreover, participants were seen 3 months after the passing of their spouse. This is a relatively uncommon study design and may illuminate early opportunities for intervention which were previously overlooked.

These strengths must be considered in light of the study's weaknesses. With a lack of a comparison group, it is difficult to determine whether or not the stress of bereavement was driving the relationship between attachment anxiety and inflammation, particularly given that social anxiety more generally is associated with chronic inflammation (e.g., Vogelzangs et al., 2013). Importantly, although attachment anxiety was associated with inflammation in the current sample, global anxiety was not, suggesting that the attachment system may indeed be at play in this bereavement context. Interestingly, our attachment anxiety findings contrast with Gouin and colleagues' (2009) findings–attachment anxiety did not predict inflammatory responses to an experimental marital conflict, where participants were specifically asked to avoid discussing topics with their partner that would lead to marital dissension (Gouin et al., 2009); hence, although the experimental stressor involved conflict, there was no threat of losing their relationship partner. Attachment theory stipulates that the impact of attachment style on individual differences in responses to stress is strongest in situations eliciting threat in attachment relationships (Bowlby, 1980). Further, attachment anxiety is characterized by a preoccupation with the partner's accessibility and excessive worry about rejection and abandonment. Thus, the death of a spouse characterizes an anxiously attached individual's worst fear coming true. Because of this, we surmise the distress associated with bereavement for those high in attachment anxiety would exacerbate any existing association between attachment anxiety and inflammation. Future research should directly test this possibility.

The current study solidifies an important first step in identifying individual difference factors that may influence loss outcomes. Due to the cross-sectional nature of this study, however, we were unable to examine loss outcomes over time. Future work should examine the time course of bereavement-related changes in inflammation as it relates to attachment anxiety. If subsequent studies utilizing multiple bereaved samples demonstrate consistent findings and further identify key time points of intervention during the grief period, this work may have important clinical implications.

While the research literature on attachment and inflammation continues to expand, attachment processes may impact inflammation differently across the lifespan, depending on a variety of demographic factors such as age, race, and social status. Among adolescents with a history of involvement in child protective services, those with insecure or disorganized attachment styles in infancy had higher levels of CRP in early childhood, compared to those with secure attachment at infancy (Bernard et al., 2019). Interestingly, African American adolescents (approximately 12 years old) who perceived their parents as secure base supports had lower CRP levels at age 32; in contrast, whether or not young adults (approximately 20 years old) perceived their parents as secure base supports did not predict CRP levels at age 32 (Jones et al., 2017). These conflicting findings indicate that the relationship between attachment and inflammatory processes may differ across the lifespan, and also may depend on the relationship context (e.g., relationship with an attachment figure that is a parent vs. a romantic partner), and developmental period (i.e., infancy, adolescence, early adulthood, late adulthood). More data is needed in order to better disentangle the differences between attachment orientations and their relationship to inflammatory processes in different contexts. In addition, the current study's sample was predominately White, with the majority attending some form of college, a limitation that should be addressed in future work, as individuals with minority status and/or those who are from lower socioeconomic status, may respond differently to the stress of losing a spouse.

This study provides additional evidence of the need for both patients' mental and physical health to be addressed. Particularly, by assessing a patient's relationships and approach to engaging with others (i.e., attachment orientation), health care providers can better identify at-risk patients for poor loss adjustment following the death of a spouse. Early resources for mental health services, pharmacological or mind-body interventions may help insulate vulnerable patients from symptoms of poor mental and physical health and potentially lower inflammation amongst at-risk bereaved individuals. Susceptibility to inflammation-driven conditions like cardiovascular disease, coronary heart disease, stroke, and cancer may be prevented by early intervention.

5. Conclusions

One of the most intuitively appealing aspects of attachment theory is that individual differences in attachment orientation serve as a template for how people respond to emotionally taxing situations throughout life (e.g., Diamond et al., 2008). Chief among these situations is the bereavement experience from spousal loss. Our results complement other work showing a relationship between high attachment anxiety and biologically relevant health outcomes (i.e., lower T-cell numbers; Jaremka et al., 2013). Armed with knowledge of a patient's relationships and approach to engaging with others (i.e., attachment orientation), health care providers could better identify at-risk patients for poor loss adjustment following the death of a spouse, creating the opportunity for early intervention during this critical and distressing life event. Future research should elucidate the impact of attachment avoidance on poor loss adjustment over a longer period after losing a spouse.

Declaration of Competing Interest

There are no conflicts of interest to declare.

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