RUNNING HEAD: TIME SPENT CO-PRESENT WITH PARTNER AND C-REACTIVE PROTEIN

Everyday co-presence with a romantic partner is associated with lower C-reactive protein

Tatum A. Jolink[1], Baldwin M. Way[2], Ayana Younge[3], Christopher Oveis[4], & Sara B. Algoe[1]

[1] Department of Psychology & Neuroscience, University of North Carolina at Chapel Hill, Chapel Hill, NC USA

[2] Department of Psychology, Institute for Behavioral Medicine Research, The Ohio State University, Columbus, OH USA

[3] Kenan-Flagler Business School, University of North Carolina at Chapel Hill, Chapel Hill, NC USA

[4] Rady School of Management, University of California, San Diego, San Diego, CA USA

Address correspondence to:
Sara B. Algoe
Department of Psychology & Neuroscience
University of North Carolina at Chapel Hill
235 E. Cameron Ave. CB #2370
Chapel Hill, NC 27599-3270
algoe@unc.edu

Declarations of interest: none

Word Count: 4,717

Abstract

Social relationships are an important driver of health, and inflammation has been proposed as a key neurobiological mechanism to explain this effect. Behavioral researchers have focused on social relationship *quality* to further explain the association, yet recent research indicates that these effects may not be as robust as previously thought. Here, building on animal models of social bonds and recent theory on close relationships, we instead investigated merely being in the physical presence of one's romantic partner. Specifically, we tested the hypothesis that spending more time co-present with a loved partner in everyday life would be associated with lower c-reactive protein (CRP). Three times over the course of one month, 100 people in romantic relationships reported how much time they spent in the same physical space as their partner in the prior 24 hours, in minutes, and provided a sample of blood for CRP assay (*n* observations = 296). Results from multi-level models showed that when one reported spending more time in the physical presence of their partner they had lower CRP – an effect that was robust to alternative explanations from the prior literature, including romantic relationship quality, hostility, and loneliness. These findings move past global assessments of social isolation to consider a novel everyday behavior that is of great interest in the non-human animal literature – spending time together - as a potential mechanism linking high-quality relationships and physical health in adult humans. The findings also point to future research on additional behavioral mechanisms that are not dependent on stress pathways: people in high-quality relationships tend to spend enjoyable and affectionate time with one another, which may impact inflammation.

Keywords: inflammation, social relationships, C-reactive protein, social behavior, pair bond, relationship quality, physical proximity

Close social connections confer benefits to physical health that include reduced mortality rates (Holt-Lunstad et al., 2010). Inflammation is one widely-proposed biological pathway through which close social connections contribute to physical health and lower mortality (Kiecolt-Glaser et al., 2010; Leschak & Eisenberger, 2019; Uchino et al., 2018). Understandably, then, quite a bit of research has focused on how the *quality* of those relationships may affect systemic inflammation. For example, researchers have identified hostility (Brooks et al., 2014; Kiecolt-Glaser et al., 2005; Yang et al., 2014), perceptions of support (Jiang et al., 2021; Kiecolt-Glaser et al., 2010; Lee & Way, 2019; Uchino et al., 2018), and even loneliness (Hawkley & Cacioppo, 2003) as being associated with inflammation. Critically, however, recent work has failed to replicate the link between distress within romantic relationships and systemic inflammation (Bajaj et al. 2016; Jaremka et al., 2020; Nilsson et al., 2020), and thus, exactly *how* close relationships could impact the immune system requires further investigation. Here, rather than quality, we focus on what we believe to be an empirically overlooked factor in the human literature on relationships and systemic inflammation: time spent in the physical presence of a loved partner.

There are many reasons to focus on physical co-presence. The first two relate to the fact that close relationship partners are a key structural element of humans' everyday lives. First, growing evidence suggests that simply being physically co-present with a loved partner reduces the need for vigilance to threats (Coan et al., 2006; 2017) and increases physiological regulation of the endocrine (i.e. hypothalamic-pituitary-adrenal axis or HPA) and autonomic pathways that influence peripheral inflammation (Beckes & Coan, 2011; Bourassa et al., 2019; Coan & Maresh, 2015; Cornelius et al., 2020; Gump et al., 2001; Han et al., 2021; Phillips et al., 2006).

Second, *how* people in non-distressed relationships tend to spend their time together involves a wide variety of relationship processes largely overlooked in the inflammation literature, which tends to focus on distressing moments (Robles & Kiecolt-Glaser, 2003): relatively satisfying relationships are characterized by interactions that are positively-valenced and affectionate or caring, which may be salubrious in their own right (cf. Algoe, 2019). In short, in *high-quality* relationships, people tend to simply spend more time with one another in a variety of ways (e.g., Chang, Way, Sheeran, Kurtz, Baucom, & Algoe, under review), making time spent co-present with a partner one logical factor to take seriously as a potential explanatory mechanism linking close relationships and systemic inflammation.

Third, although time spent physically present with a relationship partner has not been a focal relationship behavior in the human literature, it is regularly used as a marker of a close bond in the non-human animal literature (e.g., Harbart et al., 2020; Lim & Young, 2006; Silk, 2007; Williams et al., 1992), including the theorizing that this time spent co-present with a familiar (close) other helps explain reproductive fitness and longevity (Silk, 2007).

Fourth, in humans, broad-based measures of social *isolation*, which is not specific to what happens within a given relationship but reflects a potential pattern of a lack of contact (that is, *lack* of time spent co-present) with other humans across relationships, provide indirect evidence that this is a path worth pursuing: social isolation has been associated with greater inflammatory markers, such as C-reactive protein (CRP) and interleukin-6 (IL-6) (Heffner et al., 2011; Smith et al., 2020; Yang et al., 2013).

In the everyday ebb and flow of ongoing adult relationships, people have discretion about how much time they spend in the physical presence of the partner. Here, we focus on time spent with romantic relationship partners because these social partners have a large opportunity for

influence on proximal measures of health, such as systemic inflammation, due to the fact that their social contact tends to be frequent and it is consequential. People are invested and care about romantic partners (Algoe & Jolink, 2021), who are thus logically more likely to influence physiological patterns relative to many other members of one's social network. Regarding time spent co-present with romantic partners, people can make dates, eat meals together, and even if living under the same roof, can choose to be home or not, or go to bed at the same time or not, as their partner. In non-clinically distressed or depressed samples of couples such as those represented in prior literature (Bourassa et al., 2019; Coan et al., 2006; 2017; Han et al., 2021), a romantic partner can represent a source of safety (Campa et al., 2009; Collins & Feeney, 2000; Eisenberger et al., 2011). Does more time spent co-present with romantic partners then translate to lower markers of chronic distress in the body?

In the current study, we examined the effect of reported time spent co-present with a romantic partner on systemic inflammation, measured using assay of CRP levels in blood, three times over one month. CRP levels are not static, so having three samples per person increases statistical power to test the association using multi-level statistical modeling. As an acute phase protein, CRP is synthesized and released in response to pathogens and psychological factors (Pepys & Hirschfield, 2003). In studies of inflammatory clinical conditions, such as rheumatoid arthritis, such intraindividual fluctuations in CRP have been evaluated as a marker of disease state and treatment response (England et al., 2019). There has been comparatively little investigation of everyday psychosocial influences on repeated measures of peripheral CRP in non-clinical samples, which is the focus of the present study. Accordingly, we predicted greater time spent with the partner in the last 24 hours would be associated with lower CRP.

We tested this using the strength of a repeated measures design, sampling both time spent with the partner and CRP three times across four weeks.[1] Specifically, participants reported time spent in the physical presence of their partner over the 24 hours prior to the blood sample collection. We believed a 24-hour recall would be more accurate than estimating time spent throughout the past week. Additionally, this 24-hour recall was proximal to the participant's blood draw and a reasonable approximation of the participant's typical pattern of behavior, especially as one of multiple measurement points. Finally, this 24-hour time point shows good correspondence with the kinetics of CRP. Across laboratory manipulations of systemic inflammation using either lipopolysaccharide injection (Heinzl et al., 2020; Hudgins et al., 2003; Mehta et al., 2010) or Salmonella typhi vaccination (Padfield et al., 2010; Paine et al., 2013), CRP levels consistently reach their peak 24 hours after injection. To assess the relative importance of physical co-presence with the partner, we also ran analyses controlling for weekly relationship satisfaction, hostility with the partner, and individual loneliness. Finally, we also tested the reverse-causal explanatory pathway.

Methods

Participants

Individuals (N = 159, ages *range* = 18-55) who had been in a romantic relationship for at least six months were recruited from the greater Chapel Hill, North Carolina area for a study examining "Everyday Social Behavior and Health", conducted October – December 2017. Recruitment and enrollment were conducted online via Informational Email to staff and students

[1] Note that our theorizing is about high-quality, loving relationships providing a source of safety. Whereas there is a large body of clinical literature on distressed couples (cf. Baucom et al., 1998; Christensen et al., 2004), people who sign up for non-therapeutic studies like this one tend to be in loving, satisfied romantic relationships. Thus, the sample – relative to other research samples of romantic couples -- was expected to meet the threshold of our theoretical assumption.

of UNC-Chapel Hill, Researchmatch.com, jointheconquest.com, and flyers. Interested participants completed an online screening questionnaire that determined eligibility and obtained initial consent. Participants had to be at least 18 years of age and were excluded if they were pregnant or nursing, currently or within the past six months, had arthritis, rheumatoid arthritis or joint problems, had an immune disorder, auto-immune disorder, or chronic disease of the endocrine system, were diabetic, or were currently or regularly taking anti-inflammatory medication.

Based on an administrative error, participants who considered themselves to be in long distance relationships were admitted into the study. Because study hypotheses about inflammation are contingent upon participants interacting with their partners *in person*, at the final in-lab visit we asked two questions assessing whether the participant had had the opportunity to be physically present with their partner: 1) "Are you in a long distance relationship?" (Answer options: *yes* or *no*); 2) "Does your partner typically live in this area? (Greater Research Triangle area including Chapel Hill, Durham, Raleigh, and Carrboro)?" (Answer options: *yes* or *no*). To be conservative, we only included people who implied in *both* responses that they were *not* in a long distance relationship *and* that their partner lived locally (N = 100). All other responses (N = 59) were excluded from analyses. In an *a priori* power analysis conducted using G*Power, a target sample size of 98 participants was estimated to have 80% power to detect a small effect (f = 0.1) across three repeated measures. See Table 1 for descriptive characteristics of the final sample of 100 participants. Demographic characteristics of the full sample and exploratory analyses using the full sample can both be found in the Supplemental Material (SM); conclusions hold.

Table 1

Sample Characteristics.

	M (*SD*)	% (*n*)
Age	25.45 (8.13)	
Biologically Female		82% (82)
BMI	24.38 (4.07)	
Race/Ethnicity[1]		
White/Caucasian		82% (82)
Black/African American		6% (6)
Hispanic		2% (2)
Latino		2% (2)
East Asian		8% (8)
South Asian		6% (6)
Pacific Islander or Native Hawai'ian		1% (1)
Education Level[2]		
High school graduation or equivalent		5% (5)
Some college		46% (46)
College graduation		33% (33)
Professional/post-graduate degree		16% (16)

[1]Groups are not mutually exclusive as participants could endorse more than one race/ethnicity.
[2]We note education level may be confounded with age in this sample ($r = .71$, $p < .001$)

Procedure

Eligible participants were scheduled for a set of three in-lab appointments. The appointments occurred at the same time of day and day of the week, at study entry (baseline/Time 1), two weeks later (Time 2), and again four weeks later (Time 3). The primary purpose of the lab visits was to obtain a blood sample in order to measure systemic inflammation, as indexed by C-reactive protein (CRP). At each appointment, participants were greeted by an experimenter who took the participant's height and weight, pricked the participant's finger with a small lancet, and collected drops of blood on a protein saver card. Then, the participant was escorted to another private lab room to complete confidential online questionnaires. These questionnaires assessed factors that may have influenced blood work that day (e.g., medication use, smoking), then regular behavioral and psychological factors of interest for the research questions. This includes the key independent measure of how much time

participants spent in the physical presence of their partner in the prior 24 hours. The visit typically took 20-30 minutes. The day prior to attending the first and final lab sessions, participants completed longer online questionnaires; they also completed brief online questionnaires at weeks 1 and 3 from home; these additional measures are not relevant to the present study. Of the 100 eligible participants who attended the first lab visit, only one participant did not attend or provide survey data at the second lab visit and all 100 attended the third lab visit (299 viable in-lab visits/surveys total).

Measures

Total time spent co-present with partner in past 24 hours. At each measurement point, participants estimated the amount of time spent co-present with their partner in the past 24 hours (i.e., "you were in the same room with the person, whether awake or sleeping"). Time spent co-present ranged from 0 – 1440 minutes (*M* time 1 = 490.1 minutes; *M* time 2 = 521 minutes; *M* time 3 = 545.7 minutes). Data was missing from this item for two reports (*n* = 297).

Alternative explanations. At each time point, we assessed three constructs of interest in the broader literature on relationships and inflammation: relationship quality, hostility, and loneliness. To assess *relationship quality,* participants reported how terrible (*1*) to terrific (*9*) their relationship with their partner was, "on average, over this past week". Confirming our assumption that these were individuals in satisfied relationships, the average rating across all people at all time points was 7.43 (*SD* = 1.5); the modal response was 8 (*N* = 96 out of 298). *Hostility* was measured with three items, measured from not at all (*0*) to very much (*6*): "I fought with my partner this week"; "I was upset with my partner this week"; "At times this week, I felt like screaming at my partner". On average, hostility was rather low at 1.02 (SD = 1.28) across all people at all time points. Participants also reported on feelings of *loneliness* in the past week (*M*

= 1.55, *SD* = 0.56), with the average of three items measured from hardly ever (*1*), some of the time (*2*), and often (*3*): "How often do you feel that you lack companionship?"; "How often do you feel left out?"; "How often do you feel isolated from others?". We test models controlling for these variables. One participant was missing responses to all alternative explanation items (*n* = 298).

Covariates. We controlled for sociodemographic and health factors known to be associated with inflammation. All analyses controlled for biological sex, age, baseline BMI and anti-inflammatory use prior to providing their blood sample, specifically probing, "did [the participant] take over-the-counter medications for a cold, flu, or any infection in the last 24 hours?" (O'Connor et al., 2009). No data were missing from any covariate measure except the use of anti-inflammatory medicine at the second lab visit, of which a response was missing from one participant (*N* = 98).

In ancillary analyses, we also included covariates of race/ethnicity, contraceptive use, and use of anti-depressants.

C-reactive protein. C-reactive protein (CRP) was measured via dried blood spots, a method which shows excellent correspondence with CRP concentrations assayed via traditional venipuncture (McDade et al., 2004). For collection, the participant's finger was swabbed with alcohol and then pricked with an 18-gauge needle (Owen Mumford Unistick 3). Blood drops were collected on a Whatman 903 Protein Saver Card. Samples were dried for 24 hours and then punched using a 3mm Biopsy Punch (Henry Schein) and stored in microcentrifuge tubes at -80°C until assay. Samples were shipped on dry ice to the Analytical and Development Laboratory at the Ohio State University (https://ccts.osu.edu/content/ccrm-crc-analytical-specimen-labs) for analysis. Following procedures from McDade, Burhop, & Dohnal (2004), a

single 3mm punch was thawed and 200µL of buffer (phosphate-buffered saline with 0.1 percent Tween 20) was added followed by overnight (~16 hours) incubation at 4°C while shaking at 60 rpm. The following morning, eluate was diluted 1:10 and two separate 25µl aliquots (due to experimenter error, one sample was not processed in duplicate) were assayed according to the manufacturer's instructions using the Meso Scale Delivery Vplex Plus Kits (K151STG). Manufacturer provided low and high standards were run in each of the 12 plates. Across all 12 plates, the intraassay coefficient of variation was 1.95%, while the interassay coefficient of variation was 3.24%. Blood was not attained for one participant at the third lab visit. All processed samples were successfully assayed and were well within the linear range (across all plates, the lowest sample averaged 3.19 the lowest standard). Additionally, two CRP values greater than 10 ug/mL were removed from analyses, as they may indicate an acute infection (Pearson et al., 2003),[2] resulting in 296 total observations of CRP. As is common with inflammatory markers (Jaremka et al., 2020; Lee & Way, 2019; Nilsson et al., 2020), CRP values were right skewed, so the variable was log-transformed before analyses. CRP was reliably and positively associated with BMI at every time point: Time 1 $r = .33$, $p < .001$; Time 2 $r = .28$, $p = .006$; Time 3 $r = .30$, $p = .002$.

Data analysis plan

This is a within-subjects design with three repeated measures, so we used multilevel analyses to test the association between time spent in the physical presence of the partner and CRP. Linear mixed models were conducted using lmer from the lme4 package in R (Bates et al., 2014). All models used maximum likelihood estimates where intercepts were allowed to vary randomly, but slopes were fixed. Full model results can be found in SM.

[2] Sensitivity analyses including individuals with high CRP (>10 ug/mL) can be found in Supplemental Material.

In addition to the above models using the raw time spent value, to further facilitate interpretation using this powerful inferential design, we probed week to week fluctuations of time spent. Specifically, the average time spent across the three time points was calculated for each participant. That value – the participant's grand mean – was then subtracted from each time point's time spent values (Paccagnella, 2006) using the center function in the misty package in R (Yanagida, 2020). These three new values are interpreted as the amount of time spent relative to the participant's average, such that positive values reflect spending *more* time with their partner than the participant's own average and negative values reflect spending *less* time with their partner than their own average across the three measurements. The statistics from these supplementary models are reported in the SM. Finally, we explored whether a specific portion of the time spent together -- time spent co-sleeping – alone predicted CRP; those additional models are reported in the SM.

Results

See Table 2 for zero-order correlations of the main study variables and covariates at each time point.

Table 2

Bivariate Correlations with Time Spent Co-Present, CRP, and Sociodemographic Covariates.

	1	2	3	4	5	6	7	8	9
1. CRP Time 1	--								
2. CRP Time 2	.82***	--							
3. CRP Time 3	.82***	.82***	--						
4. Time spent T1	.01	.04	.04	--					
5. Time spent T2	-.02	-.06	-.07	.63***	--				
6. Time spent T3	.02	.02	-.07	.52***	.54***	--			
7. Biological sex	.20*	.17	.21*	.02	-.07	-.05	--		
8. Age	.12	.14	.10	.25*	.17	.19	.06	--	
9. BMI	.33***	.28**	.30**	.04	.04	-.08	-.07	.39***	--

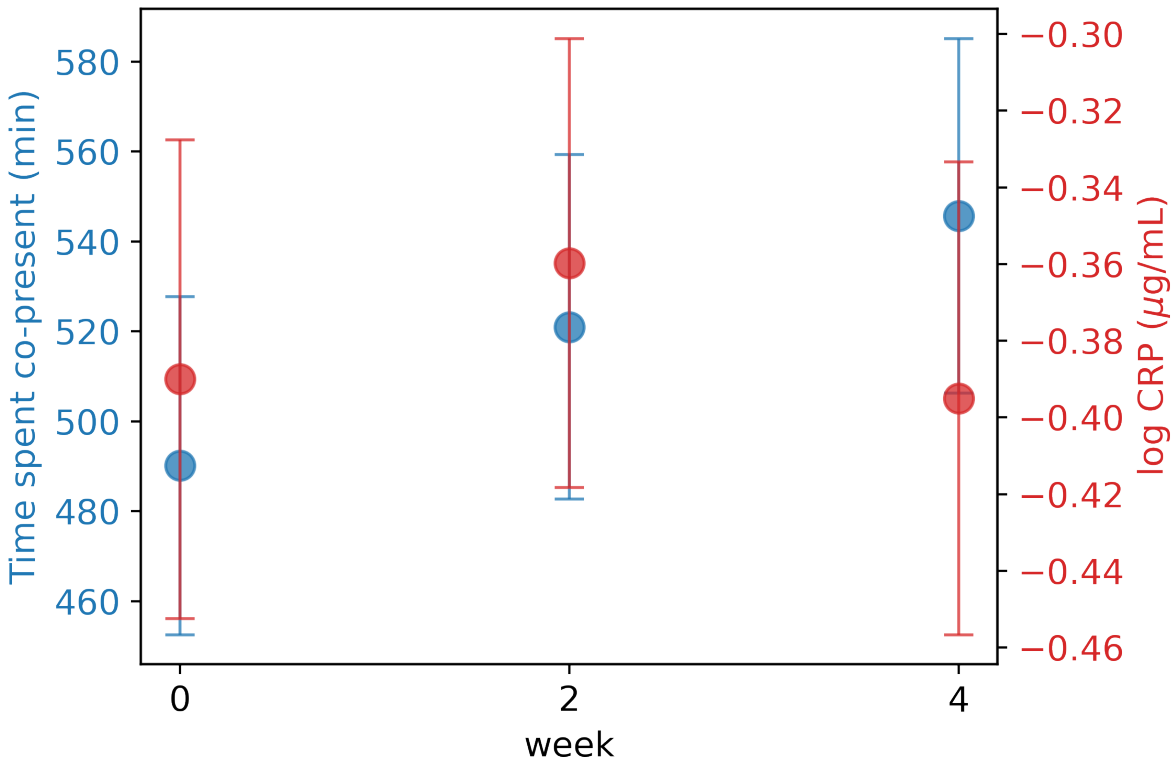
*p <.05, **p <.01, ***p <.001

Note: Time spent are raw values, in minutes. CRP are log-transformed. T = time point.

Is time spent in the physical presence of the partner associated with CRP?

Consistent with our hypotheses, the more time participants spent co-present with their partner in the prior 24 hours, the lower the participant's CRP, b = -.0001, r = 0.13, p = .043, CI95% [-.0003, -.00001]. The model controlled for standard sociodemographic and health covariates of biological sex, age, BMI, and recent anti-inflammatory use. Additionally, results remain consistent when also accounting for race and/or ethnicity, anti-depressant use, and birth control use. See SM for full statistical report. See Figure 1 for a dual axis plot of means at each time point.

Figure 1



Note. Dual-axis plot depicting mean levels of raw time spent co-present (in minutes) and log-transformed CRP values at each time point. Error bars represent the unbiased standard error of the mean.

Weekly fluctuations of time spent. In supplementary analyses, we found similar results using mean-centered deviation scores, where the value of time spent reflected participant's *deviation* from their overall average. More time spent co-present with their partner in the prior 24 hours, beyond their average across three time points, was significantly associated with participant's lower CRP, b = -.0002, r = 0.16, p = .029, CI95% [-.0003, -.00002]. Models once again controlled for biological sex, age, BMI, and recent anti-inflammatory use, and hold when also accounting for race and/or ethnicity, anti-depressant use, and birth control use. See SM for full model results.

Testing the reverse pathway: inflammation to time spent co-present. We did not find evidence of the reverse direction, such that CRP did not predict the time spent together in the prior 24 hours, accounting for biological sex, age, BMI and anti-inflammatory use (see SM).

Addressing alternative explanations: relationship quality, hostility toward partner, and loneliness

The association between total time spent co-present and CRP robustly held when controlling for each potential alternative explanation. Time spent co-present significantly negatively predicted CRP, b = -.0001, r = .13, p = .04, CI95% [-.0003, -.00001], when controlling for relationship quality that week, b = .01, r = .03, p = .67, CI95% [-.02, .04]. Time spent co-present was significantly negatively associated with CRP, b = -.0001, r = .12, p = .05, CI95% [-.0003, .0000001], when controlling for hostility with the partner that week, b = -.04, r = .13, p = .04, CI95% = [-.07, -.002]. Lastly, time spent co-present was significantly negatively associated with CRP, b = -.0001, r = .13, p = .032, CI95% [-.0003, -.00001], when controlling for loneliness that week, b = -.06, r = .08, p = .20, CI95% [-.15, .03]. Each model controlled for biological sex, age, BMI and anti-inflammatory use. Full statistics can be found in the SM,

including main effects models of each alternative explanation predicting CRP without time spent in the model.

Weekly fluctuations of time spent. Supplementary analyses show that, at a given time point, more time spent co-present with one's partner relative to one's own average was negatively significantly associated with CRP, when controlling for weekly relationship quality, hostility with the partner, and loneliness. Full model results, including controlling for biological sex, age, BMI, and anti-inflammatory use, can be found in SM.

Discussion

The present study examined how time spent co-present with a romantic partner relates to systemic inflammation, measured with CRP. Specifically, for the first time to our knowledge, we showed that simply spending more time in the physical presence of a partner was associated with lower levels of CRP the next day. We showed this using three time points sampled from across the course of a month. Indeed, supplementary analyses showed that at assessments when the participant had spent more time with the partner than their own average, they had lower CRP. Moreover, we put time spent co-present head-to-head with commonly studied explanations for links between social relationships and inflammation in the health literature – relationship quality, hostility, and loneliness – showing that total time spent co-present consistently predicts CRP, regardless of these other factors. These findings reveal a largely unexplored potential pathway through which close relationships may affect health.

The findings for time spent co-present are largely consistent with the social isolation literature (Heffner et al., 2011; Smith et al., 2020; Yang et al., 2013) but push it further. First, using the context of some of humans' most important relationships – those with a romantic partner – we show in a fine-grained way that one possible mechanism for effects of isolation is

not being physically co-present with people. More broadly, we emphasize that, whereas excellent work has demonstrated the potential buffering effects of a partner's presence on physiological outcomes during times of distress (e.g., Bourassa et al., 2019; Coan et al., 2006; Feeney & Kirkpatrick, 1996), here, we do not make the assumption that stress-buffering is the mechanism. For example, in addition to stress buffering that may happen throughout a 24-hour period, social baseline theory suggests that being alone *heightens* vigilance, whereas co-presence may be the "baseline" optimal state (Gunnar et al., 1996; Heffner et al., 2011; Smith et al., 2020; Yang et al., 2013).

Research on positive interpersonal processes emphasizes that people in high-quality relationships (like the people in our sample) tend to have social interactions with one another that are emotionally positively-valenced and caring (not negative and hostile) (Algoe, 2019), which could be salubrious in their own right, through positive emotions (Cohen & Pressman, 2006; Folkman & Moskowitz, 2000; Pressman et al., 2019), physical affection (Holt-Lunstad et al., 2008; Thomas & Kim, 2021), or other unknown mechanisms. So, in addition to time spent co-present as a new potential avenue of inquiry in this literature, we believe these data push health researchers to carefully examine features of relationships that happen the most *frequently* in everyday life (e.g., shared laughter, calm or happy states). Even if the momentary impact of such features were to be less intense than that of distress or hostility, for example (see Baumeister et al. 2001), frequency should undergird the *cumulative impact* of being in a high-quality relationship on health; biological mechanisms stemming from such moments might include physiological benefits from affectionate touch or physiological attunement (e.g., while co-sleeping), among others.

We acknowledge that our data are correlational, so although we hypothesize causality, we await stronger tests of the causal hypothesis. Further, there is theory and evidence related to the reverse direction explanation. For example, early theory suggested that the release of pro-inflammatory cytokines is associated with the prototypical "sickness behavior" of social withdrawal, and some human studies provide initial support for that using a broad array of relationship types (Eisenberger et al., 2009; 2010; Inagaki et al., 2012). However, newer theorizing suggests that whether one withdraws may depend on the specific social target, or who the relationship partner is (Muscatell & Inagaki, 2021), with the potential for people to want to *approach* close partners, such as romantic partners. Indeed, studies show heightened inflammation is associated with or causes people to more readily approach close relationship partners (Inagaki et al., 2015; Jolink et al., 2021). Those new data would suggest that if inflammation was causing social behavior, one would expect to see a significantly *positive* association between CRP and time spent co-present with the partner, not the significant negative association that we show in the present study. Finally, our test of CRP predicting time spent with the partner was not significant. Altogether, we believe our theoretical explanation to be a better match to the present data than the reverse causal pathway, but we await further testing.

Our findings add to the evidence base regarding associations between various measures of social relationship quality and inflammation (Holt-Lunstad et al. 2010; Smith et al. 2020; Uchino et al 2018). Romantic relationship quality and loneliness were not associated with CRP in our sample, despite associations with inflammation in the prior literature (Bajaj et al. 2017; Gouin et al., 2016; Hawkley et al. 2007; Jaremka et al. 2013; Kiecolt-Glaser et al. 2010; Ross et al. 2017; Shankar et al 2011). Additionally, we were somewhat surprised to find that hostility significantly predicted CRP in the opposite direction as the prior literature would suggest, both

with and without time spent co-present with the partner in the model: While much of the existing literature suggests hostility and strain in close relationships are associated with greater inflammation (Brooks et al., 2014; Gouin et al., 2009; Kiecolt-Glaser et al., 2005; 2010; Yang et al., 2014), in this case, hostility was associated with lower inflammation (see Bajaj et al., 2016 for one similar finding). We note that other recent research focusing on negatively-valenced aspects of relationship functioning also raises questions about the strength of association with CRP (e. g., Jaremka et al., 2020) or relevant moderating variables in the link between conflict and inflammation (e.g., synchrony in heartrate variability, Wilson et al. 2018). Moving forward, the results for hostility should be interpreted in the context of the present study, with the primary contextual factor being that these are quite satisfied couples. Hostility ratings were quite low (see Method); however, it is natural for people to get on one another's nerves and plenty of research from affective, clinical, and relationship science suggests that acknowledging negative emotions is healthy (Blackledge & Hayes, 2001; John & Gross, 2004; Overall & McNulty, 2017; Torre & Lieberman, 2018). We look forward to future work that unpacks the meaning of especially low self-reports of hostility (or conversely, modestly higher reports in this happy context), or what else might be happening for the couple when hostility is at its nadir, as these insights might guide future predictions regarding inflammation.

We also draw attention to three opportunities for additional research. First, we believe the relationships of participants in this study cross a threshold for feelings of care and safety that underlies our theoretical assumption about the potential value of time spent co-present on inflammation. However, research in distressed couples remains warranted to further refine the theorizing: one possibility, drawn from social baseline theory (Beckes & Coan, 2011), is that even poor relationships still offer slightly more benefit than being alone. Alternatively,

relationships with greater stress and negative affect may not. That question needs empirical testing. Second, the time spent co-present variable was self-reported by participants. A prior study using this same measure independently reported by both couple members for 35 nights showed corroboration about the validity of participants' time estimates: there was minimal variance between partners in these reports (Chang et al., under review). That said, there are likely other objective measures of time spent in physical co-presence that would help to augment future study designs. Third, these effects may not be unique to CRP, so future work should examine physical co-presence and other markers of inflammation to ensure that the effects on CRP are indeed due to peripheral inflammation and not another biological process (Del Guidice & Gangestad, 2018).

People with whom we are in close social relationships, such as a quality romantic partner, are who we want to laugh with, who we want to hug, or who we choose to sit in silence and stillness next to at the end of the day. Enduring, elevated systemic inflammation, as reflected by continued production of higher CRP levels, can produce poor health outcomes (Ershler & Keller, 2000; Kiecolt-Glaser et al., 2010; Ridker, 2009). We sampled CRP on three different days across time to find evidence suggesting merely being together with a romantic partner is beneficial in the form of lower CRP. By identifying this proximal biological pathway through which being with our closest others may facilitate better health outcomes, these findings reveal yet uncharted avenues for addressing the mechanisms through which close relationships affect long-term health.

Acknowledgements

This work was supported by a John Templeton Foundation Grant (#56458) awarded to Dr. Algoe. The authors are grateful to the participants for their contributions and our hardworking research assistants who helped make the study possible.

References

Algoe, S. B. (2019). Positive interpersonal processes. *Current Directions in Psychological Science*, *28*(2), 183-188.

Algoe, S. B., & Jolink, T. A. (2020). Social bonds: A new look at an old topic. *Social psychology: Handbook of basic principles*, 140-162.

Bajaj, A., John-Henderson, N. A., Cundiff, J. M., Marsland, A. L., Manuck, S. B., & Kamarck, T. W. (2016). Daily social interactions, close relationships, and systemic inflammation in two samples: Healthy middle-aged and older adults. *Brain, behavior, and immunity*, *58*, 152-164.

Bates, D., Mächler, M., Bolker, B., & Walker, S. (2014). Fitting linear mixed-effects models using lme4. *arXiv preprint arXiv:1406.5823*.

Baucom, D. H., Shoham, V., Mueser, K. T., Daiuto, A. D., & Stickle, T. R. (1998). Empirically supported couple and family interventions for marital distress and adult mental health problems. *Journal of consulting and clinical psychology*, *66*(1), 53.

Baumeister, R. F., Bratslavsky, E., Finkenauer, C., & Vohs, K. D. (2001). Bad is stronger than good. *Review of general psychology*, *5*(4), 323-370.

Beckes, L., & Coan, J. A. (2011). Social baseline theory: The role of social proximity in emotion and economy of action. *Social and Personality Psychology Compass*, *5*(12), 976-988.

Blackledge, J. T., & Hayes, S. C. (2001). Emotion regulation in acceptance and commitment therapy. *Journal of clinical psychology*, *57*(2), 243-255.

Bourassa, K. J., Ruiz, J. M., & Sbarra, D. A. (2019). The impact of physical proximity and attachment working models on cardiovascular reactivity: Comparing mental activation and romantic partner presence. *Psychophysiology*, *56*(5), e13324.

Brooks, K. P., Gruenewald, T., Karlamangla, A., Hu, P., Koretz, B., & Seeman, T. E. (2014). Social relationships and allostatic load in the MIDUS study. *Health Psychology*, 33, 1373–1381.

Chang, Y-P., Way, B. M., Sheeran, P., Kurtz, L. E., Baucom, D. H., & Algoe, S. B. (*under review*). Promoting expressed gratitude in one member of a romantic couple increases time they spend together in everyday life.

Christensen, A., Atkins, D. C., Berns, S., Wheeler, J., Baucom, D. H., & Simpson, L. E. (2004). Traditional versus integrative behavioral couple therapy for significantly and chronically distressed married couples. *Journal of consulting and clinical psychology*, *72*(2), 176.

Coan, J. A., Beckes, L., Gonzalez, M. Z., Maresh, E. L., Brown, C. L., & Hasselmo, K. (2017). Relationship status and perceived support in the social regulation of neural responses to threat. *Social Cognitive and Affective Neuroscience*, *12*(10), 1574-1583.

Coan, J. A., Schaefer, H. S., & Davidson, R. J. (2006). Lending a hand: Social regulation of the neural response to threat. *Psychological science*, *17*(12), 1032-1039.

Coan, J., & Maresh, E. L. (2014). Social baseline theory and the social regulation of emotion. In J. Gross (Ed.), Handbook of emotion regulation (2nd ed.). New York, NY: Guilford Press.

Cohen, S., & Pressman, S. D. (2006). Positive affect and health. *Current directions in psychological science*, *15*(3), 122-125.

Cornelius, T., Birk, J. L., Edmondson, D., & Schwartz, J. E. (2020). Ambulatory Blood Pressure Response to Romantic Partner Interactions and Long-Term Cardiovascular Health Outcomes. *Psychosomatic medicine*, *82*(4), 393.

Eisenberger, N. I., Master, S. L., Inagaki, T. K., Taylor, S. E., Shirinyan, D., Lieberman, M. D., & Naliboff, B. D. (2011). Attachment figures activate a safety signal-related neural region and reduce pain experience. *Proceedings of the National Academy of Sciences*, 108(28), 11721-11726.

Eisenberger, N. I., Moieni, M., Inagaki, T. K., Muscatell, K. A., & Irwin, M. R. (2017). In sickness and in health: the co-regulation of inflammation and social behavior. *Neuropsychopharmacology*, *42*(1), 242-253.

Eisenberger, N.I., Inagaki, T.K., Mashal, N.M., Irwin, M.R. (2010). Inflammation and social experience: an inflammatory challenge induces feelings of social disconnection in addition to depressed mood. *Brain, behavior, and Immunity, 24* (4), 558–563. https://doi.org/ 10.1016/j.bbi.2009.12.009.

Eisenberger, N.I., Inagaki, T.K., Rameson, L.T., Mashal, N.M., & Irwin, M.R. (2009). An fMRI study of cytokine-induced depressed mood and social pain: the role of sex differences. *Neuroimage*, *47*(3), 881–890. https://doi.org/10.1016/j.neuroimage.2009.04.040

England, B. R., Tiong, B. K., Bergman, M. J., Curtis, J. R., Kazi, S., Mikuls, T. R., O'Dell, J. R., Ranganath, V. K., Limanni, A., Suter, L. G., & Michaud, K. (2019). 2019 Update of the American College of Rheumatology Recommended Rheumatoid Arthritis Disease Activity Measures. *Arthritis Care & Research*, *71*(12), 1540–1555. https://doi.org/10.1002/acr.24042

Ershler, W. B., & Keller, E. T. (2000). Age-associated increased interleukin-6 gene expression, late-life diseases, and frailty. *Annual Review of Medicine*, 51, 245–270. http://dx.doi.org/10.1146/annurev.med.51.1.245

Feeney, B. C., & Kirkpatrick, L. A. (1996). Effects of adult attachment and presence of romantic partners on physiological responses to stress. *Journal of personality and social psychology*, *70*(2), 255.

Folkman, S., & Moskowitz, J. T. (2000). Stress, positive emotion, and coping. *Current directions in psychological science*, *9*(4), 115-118.

Gassen, J., & Hill, S. E. (2019). Why inflammation and the activities of the immune system matter for social and personality psychology (and not only for those who study health). *Social and Personality Psychology Compass*, *13*(6), e12471.

Gouin, J. P., Glaser, R., Loving, T. J., Malarkey, W. B., Stowell, J., Houts, C., & Kiecolt-Glaser, J. K. (2009). Attachment avoidance predicts inflammatory responses to marital conflict. *Brain, behavior, and immunity*, *23*(7), 898-904.

Gouin, J. P., Scarcello, S., da Estrela, C., Paquin, C., & Barker, E. T. (2016). Dyadic coping and inflammation in the context of chronic stress. *Health Psychology*, *35*(10), 1081.

Gump, B. B., Polk, D. E., Kamarck, T. W., & Shiffman, S. M. (2001). Partner interactions are associated with reduced blood pressure in the natural environment: Ambulatory monitoring evidence from a healthy, multiethnic adult sample. *Psychosomatic medicine*, *63*(3), 423-433.

Gunnar, M. R., Brodersen, L., Nachmias, M., Buss, K., & Rigatuso, J. (1996). Stress reactivity and attachment security. *Developmental psychobiology*, *29*(3), 191-204.

Han, S. C., Schacter, H. L., Timmons, A. C., Kim, Y., Sichko, S., Pettit, C., ... & Margolin, G. (2021). Romantic partner presence and physiological responses in daily life: Attachment style as a moderator. *Biological Psychology*, 161, 108082.

Harbert, K. J., Pellegrini, M., Gordon, K. M., & Donaldson, Z. R. (2020). How prior pair-bonding experience affects future bonding behavior in monogamous prairie voles. *Hormones and Behavior*, *126*, 104847.

Hawkley, L. C., & Cacioppo, J. T. (2003). Loneliness and pathways to disease. *Brain, behavior, and immunity*, *17*(1), 98-105.

Hawkley, L. C., Bosch, J. A., Engeland, C. G., Marucha, P. T., & Cacioppo, J. T. (2007). Loneliness, dysphoria, stress, and immunity: A role for cytokines. In N. P. Plotnikoff, R. E. Faith, A. J. Murgo, R. A. Good (Eds.), Cytokines: Stress and immunity (2nd ed., pp. 67–85). Boca Raton, FL: CRC Press.

Heffner, K. L., Waring, M. E., Roberts, M. B., Eaton, C. B., & Gramling, R. (2011). Social isolation, C-reactive protein, and coronary heart disease mortality among community-dwelling adults. *Social science & medicine*, *72*(9), 1482-1488.

Heinzl, M. W., Resl, M., Klammer, C., Egger, M., Dieplinger, B., & Clodi, M. (2020). Proprotein convertase subtilisin/kexin type 9 (PCSK9) is not induced in artificial human inflammation and is not correlated with inflammatory response. *Infection and Immunity*, *88*(3), e00842-19.

Hennessy, M. B., Deak, T., & Schiml, P. A. (2014). Sociality and sickness: have cytokines evolved to serve social functions beyond times of pathogen exposure?. *Brain, behavior, and immunity*, *37*, 15-20.

Holt-Lunstad, J., Birmingham, W. A., & Light, K. C. (2008). Influence of a "warm touch" support enhancement intervention among married couples on ambulatory blood pressure, oxytocin, alpha amylase, and cortisol. *Psychosomatic medicine*, *70*(9), 976-985.

Holt-Lunstad, J., Smith, T. B., & Layton, J. B. (2010). Social relationships and mortality risk: A meta-analytic review. *PLoS Medicine*, 7, e1000316. http://dx.doi.org/10.1371/journal.pmed.1000316

Hudgins, L. C., Parker, T. S., Levine, D. M., Gordon, B. R., Saal, S. D., Jiang, X., Seidman, C. E., Tremaroli, J. D., Lai, J., & Rubin, A. L. (2003). A single intravenous dose of endotoxin rapidly alters serum lipoproteins and lipid transfer proteins in normal volunteers. *Journal of Lipid Research*, *44*(8), 1489–1498.

Inagaki, T.K., Muscatell, K.A., Irwin, M.R., Cole, S.W., Eisenberger, N.I., 2012. Inflammation selectively enhances amygdala activity to socially threatening images. *Neuroimage*, *59*(4), 3222–3226. https://doi.org/10.1016/j.neuroimage.2011.10.090.

Inagaki, T.K., Muscatell, K.A., Irwin, M.R., Moieni, M., Dutcher, J.M., Jevtic, I., Breen, E.C., & Eisenberger, N.I. (2015). The role of the ventral striatum in inflammatory-induced approach toward support figures. *Brain, behavior, and immunity*, 44, 247–252. https://doi.org/ 10.1016/j.bbi.2014.10.006.

Irwin, M. R., Olmstead, R., & Carroll, J. E. (2016). Sleep disturbance, sleep duration, and inflammation: a systematic review and meta-analysis of cohort studies and experimental sleep deprivation. *Biological psychiatry*, *80*(1), 40-52.

Jaremka, L. M., Fagundes, C. P., Peng, J., Bennett, J. M., Glaser, R., Malarkey, W. B., & Kiecolt-Glaser, J. K. (2013). Loneliness promotes inflammation during acute stress. *Psychological Science*, *24*(7), 1089-1097.

Jaremka, L. M., Kane, H. S., Sunami, N., Lebed, O., & Austin, K. A. (2020). Romantic relationship distress, gender, socioeconomic status, and inflammation: A preregistered report. *Personal Relationships*, *27*(3), 708-727.

Jiang, T., Yakin, S., Crocker, J., & Way, B. M. (2021). Perceived Social Support-Giving Moderates the Association Between Social Relationships and Interleukin-6. *Brain, behavior, and immunity*.

John, O. P., & Gross, J. J. (2004). Healthy and unhealthy emotion regulation: Personality processes, individual differences, and life span development. *Journal of personality*, *72*(6), 1301-1334.

Jolink, T. A., Fendinger, N. J., Alvarez, G. M., Feldman, M. J., Gaudier-Diaz, M. M., & Muscatell, K. A. (2021). Inflammatory Reactivity to the Influenza Vaccine is Associated with Changes in Automatic Social Behavior. *Brain, behavior, and immunity*.

Kiecolt-Glaser, J. K., Gouin, J. P., & Hantsoo, L. (2010). Close relationships, inflammation, and health. *Neuroscience and Biobehavioral Reviews*, 35, 33–38. http://dx.doi.org/10.1016/j.neubiorev.2009.09.003

Kiecolt-Glaser, J. K., Loving, T. J., Stowell, J. R., Malarkey, W. B., Lemeshow, S., Dickinson, S. L., & Glaser, R. (2005). Hostile marital interactions, proinflammatory cytokine production, and wound healing. *Archives of General Psychiatry*, 62, 1377–1384.

Lee, D. S., & Way, B. M. (2019). Perceived social support and chronic inflammation: The moderating role of self-esteem. *Health Psychology*, *38*(6), 563.

Leschak, C. J., & Eisenberger, N. I. (2019). Two distinct immune pathways linking social relationships with health: inflammatory and antiviral processes. *Psychosomatic medicine*, *81*(8), 711.

Lim, M. M., & Young, L. J. (2006). Neuropeptidergic regulation of affiliative behavior and social bonding in animals. *Hormones and behavior*, *50*(4), 506-517.

McDade, T. W., Burhop, J., & Dohnal, J. (2004). High-sensitivity enzyme immunoassay for C-reactive protein in dried blood spots. *Clinical Chemistry*, *50*(3), 652–654.

Mehta, N. N., McGillicuddy, F. C., Anderson, P. D., Hinkle, C. C., Shah, R., Pruscino, L., Tabita-Martinez, J., Sellers, K. F., Rickels, M. R., & Reilly, M. P. (2010). Experimental endotoxemia induces adipose inflammation and insulin resistance in humans. *Diabetes*, *59*(1), 172–181.

Muscatell, K. A., & Inagaki, T. K. (2021). Beyond social withdrawal: new perspectives on the effects of inflammation on social behavior. *Brain, Behavior, & Immunity-Health*, *16*, 100302.

Nilsson, C. J., Nørgaard, S., Foverskov, E., Bruunsgaard, H., Andersen, P. K., & Lund, R. (2020). Positive and negative aspects of social relations and low-grade inflammation in Copenhagen Aging and Midlife Biobank. *European Journal of Ageing*, *17*(4).

O'Connor, M. F., Bower, J. E., Cho, H. J., Creswell, J. D., Dimitrov, S., Hamby, M. E.,... Irwin, M. R. (2009). To assess, to control, to exclude: Effects of biobehavioral factors on circulating inflammatory markers. *Brain, Behavior, and Immunity*, *23*, 887– 897. http://dx.doi.org/10.1016/ j.bbi.2009.04.005

Overall, N. C., & McNulty, J. K. (2017). What type of communication during conflict is beneficial for intimate relationships?. *Current opinion in psychology*, *13*, 1-5.

Paccagnella, O. (2006). Centering or not centering in multilevel models? The role of the group mean and the assessment of group effects. *Evaluation review*, *30*(1), 66-85.

Padfield, G. J., Tura, O., Haeck, M. L., Short, A., Freyer, E., Barclay, G. R., ... & Mills, N. L. (2010). Circulating endothelial progenitor cells are not affected by acute systemic

inflammation. *American Journal of Physiology-Heart and Circulatory Physiology*, *298*(6), H2054-H2061.

Paine, N. J., Ring, C., Bosch, J. A., Drayson, M. T., & van Zanten, J. J. V. (2013). The time course of the inflammatory response to the Salmonella typhi vaccination. *Brain, behavior, and immunity*, *30*, 73-79.

Patel, S. R., Zhu, X., Storfer-Isser, A., Mehra, R., Jenny, N. S., Tracy, R., & Redline, S. (2009). Sleep duration and biomarkers of inflammation. *Sleep*, *32*(2), 200-204.

Pearson, T. A., Mensah, G. A., Alexander, R. W., Anderson, J. L., Cannon, R. O., III, Criqui, M., . . . the Centers for Disease Control and Prevention, & the American Heart Association. (2003). Markers of inflammation and cardiovascular disease: Application to clinical and public health practice: A statement for healthcare professionals from the Centers for Disease Control and Prevention and the American Heart Association. *Circulation*, 107, 499 –511. http://dx.doi.org/10.1161/01.CIR.000005 2939.59093.45

Pepys, M. B., & Hirschfield, G. M. (2003). C-reactive protein: a critical update. *The Journal of clinical investigation*, *111*(12), 1805-1812.

Phillips, A. C., Carroll, D., Hunt, K., & Der, G. (2006). The effects of the spontaneous presence of a spouse/partner and others on cardiovascular reactions to an acute psychological challenge. *Psychophysiology*, *43*(6), 633-640.

Pressman, S. D., Jenkins, B. N., & Moskowitz, J. T. (2019). Positive affect and health: what do we know and where next should we go?. *Annual Review of Psychology*, *70*, 627-650.

Ridker, P. M. (2009). C-reactive protein: Eighty years from discovery to emergence as a major risk marker for cardiovascular disease. *Clinical Chemistry*, 55, 209 –215. http://dx.doi.org/10.1373/clinchem.2008.119214

Robles, T. F., & Kiecolt-Glaser, J. K. (2003). The physiology of marriage: Pathways to health. *Physiology & behavior*, *79*(3), 409-416.

Ross, K. M., Miller, G., Qadir, S., Keenan-Devlin, L., Leigh, A. K., & Borders, A. (2017). Close relationship qualities and maternal peripheral inflammation during pregnancy. *Psychoneuroendocrinology*, *77*, 252-260.

Shankar, A., McMunn, A., Banks, J., & Steptoe, A. (2011). Loneliness, social isolation, and behavioral and biological health indicators in older adults. *Health Psychology*, *30*(4), 377.

Silk, J. B. (2007). Social components of fitness in primate groups. *Science*, *317*(5843), 1347-1351.

Smith, K. J., Gavey, S., RIddell, N. E., Kontari, P., & Victor, C. (2020). The association between loneliness, social isolation and inflammation: a systematic review and meta-analysis. *Neuroscience & Biobehavioral Reviews*, *112*, 519-541.

Torre, J. B., & Lieberman, M. D. (2018). Putting feelings into words: Affect labeling as implicit emotion regulation. *Emotion Review*, *10*(2), 116-124.

Uchino, B. N., Trettevik, R., Kent de Grey, R. G., Cronan, S., Hogan, J., & Baucom, B. R. (2018). Social support, social integration, and inflammatory cytokines: A meta-analysis. *Health Psychology*, *37*(5), 462.

Williams, J. R., Carter, C. S., & Insel, T. (1992). Partner Preference Development in Female Prairie Voles Is Facilitated by Mating or the Central Infusion of Oxytocin a. *Annals of the New York Academy of Sciences*, *652*(1), 487-489.

Wilson, S. J., Bailey, B. E., Jaremka, L. M., Fagundes, C. P., Andridge, R., Malarkey, W. B., ... & Kiecolt-Glaser, J. K. (2018). When couples' hearts beat together: Synchrony in heart

rate variability during conflict predicts heightened inflammation throughout the day. *Psychoneuroendocrinology*, *93*, 107-116.

Yanagida, T., & Yanagida, M. T. (2020). Package 'misty'.

Yang, Y. C., McClintock, M. K., Kozloski, M., & Li, T. (2013). Social isolation and adult mortality: the role of chronic inflammation and sex differences. *Journal of health and social behavior*, *54*(2), 183-203.

Yang, Y. C., Schorpp, K., & Harris, K. M. (2014). Social support, social strain and inflammation: Evidence from a national longitudinal study of US adults. Social science & medicine, 107, 124-135.

Supplemental Materials

Method: Frequencies of Medication Use Across All Three Lab Visits

Of the 298 observations on anti-inflammation medication use, 17 observations indicated using over-the-counter anti-inflammatory medication within 24-hours of providing their blood sample; 281 observations indicated not using OTC anti-inflammatory medicine. Of 300 observations, 48 observations included reported anti-depressants use; 252 observations indicated no anti-depressant use. Of 300 observations, 153 observations indicated currently using birth control while the remaining 147 observations indicated *no* birth control use.

Supplementary Table 1: Correlation Table with Total Time Spent Co-Present, CRP, and Alternative Explanation Variables

Supplementary Table 1

Raw Bivariate Correlations for All Study Variables by Time Point.

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1. CRP Time 1	--														
2. CRP Time 2	.79***	--													
3. CRP Time 3	.82***	.81***	--												
4. Time spent co-present T1	.01	.09	.05	--											
5. Time spent co-present T2	-.02	-.02	-.07	.67***	--										
6. Time spent co-present T3	-.01	.02	-.07	.57***	.73***	--									
7. Relationship satisfaction T1	.09	.14	.12	.16*	.09	.11	--								
8. Relationship satisfaction T2	.10	.13	.11	.10	.08	.07	.62***	--							
9. Relationship satisfaction T3	.04	.06	.08	.14	.12	.10	.61***	.57***	--						
10. Loneliness T1	-.02	.06	-.03	-.13	-.08	.04	-.30**	-.27**	-.27**	--					
11. Loneliness T2	.04	.11	.07	-.07	-.11	-.03	-.32***	-.35***	-.29**	.62***	--				
12. Loneliness T3	-.05	.03	-.05	.04	.06	.08	-.32***	-.30**	-.29**	.75***	.64***	--			
13. Hostility T1	-.06	.02	-.004	.005	-.01	-.02	-.59***	-.26*	-.34***	.27**	.28**	.36***	--		
14. Hostility T2	-.13	-.12	-.10	.02	.08	.04	-.28**	-.57***	-.18	.22*	.24*	.23*	.46***	--	
15. Hostility T3	-.07	-.02	-.07	-.07	-.10	-.05	-.42***	-.33**	-.71***	.28**	.28**	.34***	.60***	.34***	--

*p <.05, **p <.01, ***p <.001

Note: CRP is log-transformed variable. T = time point.

Supplementary Table 2: Descriptives of Main Study Variables

Supplementary Table 2

Means, SDs, and Ranges for All Study Variables by Time Point.

	***M* (SD)**	**Min-Max**
1. CRP Time 1	*-0.39* (.57)	-2-.82
2. CRP Time 2	*-0.33* (.59)	-1.83-0.96
3. CRP Time 3	*-0.4* (.59)	-1.89-0.98
4. Time spent co-present T1	*383.73* (415.32	0-1440
5. Time spent co-present T2	*392.19* (405.23	0-1380
6. Time spent co-present T3	*419.08* (433.04)	0-1440
7. Relationship satisfaction T1	*7.26* (1.57)	2-9
8. Relationship satisfaction T2	*7.46* (1.33)	3-9
9. Relationship satisfaction T3	*7.46* (1.66)	1-9
10. Loneliness T1	*1.74* (0.55)	1-3
11. Loneliness T2	*1.33* (0.5)	1-3
12. Loneliness T3	*1.59* (0.55)	1-3
13. Hostility T1	*1.16* (1.38)	0-6
14. Hostility T2	*0.98* (1.12)	0-4.7
15. Hostility T3	*1* (1.31)	0-6

Note: CRP values log-transformed.

Supplementary Table 3: Primary Analyses

Supplementary Table 3 shows full model results for time spent co-present predicting CRP, controlling for standard covariates of biological sex, age, BMI, and anti-inflammatory use in the prior 24 hours.

Supplementary Table 3

Total Time Spent Co-Present Predicting CRP

Predictors	*b* [95% CI]	*t*
Time spent co-present	-.0001 [-.0003, -.000004]	-2.03*
Biological sex	.34 [.07, .61]	2.47*
Age	.001 [-.01, .01]	0.09
BMI	.05 [.02, .07]	3.33**
Anti-inflammatory use	.22 [.06, .37]	2.71**

*p <.05, **p <.01, ***p <.001

Supplementary Table 4: Primary Analyses Controlling for All Covariates

Supplementary Table 4 shows full model results for time spent co-present predicting CRP, controlling for all standard covariates (see Supplementary Table 2) as well as race, birth control use, and anti-depressant use.

Supplementary Table 4

Total Time Spent Predicting CRP, Controlling for All Covariates.

Predictors	*b* [95% CI]	*t*
Time spent co-present	-.0001 [-.0003, -.00001]	-2.14*
Biological sex	.10 [-.16, .36]	0.75
Age	.01 [-.01, .02]	0.89
BMI	.05 [.03, .08]	4.43***
Anti-inflammatory use	.20 [.04, .36]	2.50*
White	.29 [-.08, .67]	1.54
Black	-.31 [-.73, .11]	-1.45
Hispanic	.78 [.05, 1.52]	2.11*
Latino	-.16 [-.90, .59]	-0.42
East Asian	-.13 [-.51, .24]	-0.68
South Asian	.43 [-.10, .95]	1.60
Hawaiian/Pacific Islander	-.45 [-1.40, .49]	-.95
Birth control use	.43 [.22, .63]	4.16***
Anti-depressant use	-.19 [-.43, .05]	-1.57

*p <.05, **p <.01, ***p <.001

Supplementary Tables 5-10: Analyses with Alternative Explanations: Relationship Quality, Hostility Toward the Partner, and Loneliness

Primary analyses (see Supplementary Table 3) were also conducted controlling for relationship quality, hostility with the partner, and loneliness. Supplementary Tables 5-7 first establish the effect of each alternative explanation from the prior literature, showing no associations between relationship quality and loneliness with CRP, but a significant negative association between hostility and CRP. Supplementary Tables 8-10 show primary analysis results of time spent co-present predicting CRP (see Supplementary Table 4) when controlling for each alternative explanation, separately.

Supplementary Table 5

Weekly Relationship Quality Predicting CRP.

Predictors	*b* [95% CI]	*t*
Relationship quality	.004 [-.03, .04]	0.27
Biological sex	.34 [.07, .61]	2.53*
Age	-.001 [-.01, .01]	-0.11
BMI	.05 [.02, .08]	3.43***
Anti-inflammatory use	.21 [.05, .37]	2.62**

*p <.05, **p <.01, ***p <.001

Supplementary Table 6

Weekly Hostility toward Partner Predicting CRP.

Predictors	*b* [95% CI]	*t*
Hostility	-.04 [-.07, -.002]	-2.08*
Biological sex	.33 [.06, .59]	2.49*
Age	.0002 [-.01, .02]	0.03
BMI	.05 [.02, .08]	3.56***
Anti-inflammatory use	.22 [.07, .38]	2.74**

*p <.05, **p <.01, ***p <.001

Supplementary Table 7

Weekly Loneliness Predicting CRP.

Predictors	*b* [95% CI]	*t*
Loneliness	-.04 [-.13, .05]	-0.95
Biological sex	.34 [.07, .61]	2.51*
Age	-.001 [-.01, .01]	-0.11

BMI	.05 [.02, .08]	3.47***
Anti-inflammatory use	.22 [.06, .38]	2.70**

*p <.05, **p <.01, ***p <.001

Supplementary Table 8

Total Time Spent Co-Present Predicting CRP, Controlling for Weekly Relationship Quality

Predictors	*b* [95% CI]	*t*
Time spent co-present	-.0001 [-.0003, -.00001]	-2.06*
Relationship quality	.01 [-.02, .04]	0.43
Biological sex	.33 [.06, .60]	2.44*
Age	.001 [-.01, .01]	0.14
BMI	.05 [.02, .07]	3.35**
Anti-inflammatory use	.21 [.06, .37]	2.68**

*p <.05, **p <.01, ***p <.001

Supplementary Table 9

Total Time Spent Co-Present Predicting CRP, Controlling for Weekly Hostility Toward Partner.

Predictors	*b* [95% CI]	*t*
Time spent co-present	-.0001 [-.0003, -.0000001]	-1.97*
Hostility	-.04 [-.07, -.002]	-2.07*
Biological sex	.33 [.06, .59]	2.42*
Age	.001 [-.01, .02]	0.24
BMI	.05 [.02, .08]	3.46***
Anti-inflammatory use	.22 [.07, .38]	2.81**

*p <.05, **p <.01, ***p <.001

Supplementary Table 10

Total Time Spent Co-Present Predicting CRP, Controlling for Weekly Loneliness.

Predictors	*b* [95% CI]	*t*
Time spent co-present	-.0001 [-.0002, -.00001]	-2.16*
Loneliness	-.06 [-.15, .03]	-1.28
Biological sex	.33 [.06, .60]	2.42*
Age	.001 [-.01, .01]	0.14
BMI	.05 [.02, .08]	3.39**
Anti-inflammatory use	.22 [.07, .38]	2.80**

*p <.05, **p <.01, ***p <.001

Supplementary Table 11: Reverse Pathway of CRP to Time Spent Co-Present

Supplementary Table 11

CRP Predicting Time Spent Co-Present in Prior 24 Hours

Predictors	*b* [95% CI]	*t*
CRP	-62.60 [-154.74, 28.33]	-1.36
Biological sex	-36.32 [-198.23, 126.66]	0.44
Age	11.23 [3.02, 19.45]	2.70**
BMI	-6.32 [-23.22, 10.70]	-0.74
Anti-inflammatory use	2.26 [-154.18, 157.53]	0.03

*p <.05, **p <.01, ***p <.001

Supplementary Table 12:
Supplementary Analyses Using Weekly Fluctuations of Time Spent

Supplementary Table 12 shows results using the supplemental group-mean-centered version of time spent co-present predicting CRP, in which numbers reflect deviations from participant's own average across the three time points. We control for standard covariates of biological sex, age, BMI, and anti-inflammatory use in the prior 24 hours.

Supplementary Table 12

Weekly Fluctuations of Total Time Spent Co-Present Predicting CRP.

Predictors	*b* [95% CI]	*t*
Time spent co-present	-.0002 [-.0003, -.00002]	-2.21*
Biological sex	.34 [.08, .61]	2.54*
Age	-.001 [-.01, .01]	-0.12
BMI	.05 [.02, .08]	3.43***
Anti-inflammatory use	.22 [.06, .38]	2.74**

*p <.05, **p <.01, ***p <.001

Supplementary Table 13: Supplementary Analyses Controlling for All Covariates

Supplementary Table 13 shows results using the group-mean-centered version of time spent co-present, controlling for all standard covariates (see Table 2 in the main text) as well as race, birth control use, and anti-depressant use.

Supplementary Table 13

Weekly Fluctuations of Total Time Spent Predicting CRP, Controlling for All Covariates.

Predictors	*b* [95% CI]	*t*
Time spent co-present	-.0002 [-.0003, -.00002]	-2.21*
Biological sex	.12 [-.14, .38]	0.88
Age	.004 [-.01, .02]	0.65
BMI	.06 [.03, .08]	4.57***
Anti-inflammatory use	.20 [.04, .36]	2.53*
White	.30 [-.09, .67]	1.53
Black	-.29 [-.72, .12]	-1.40
Hispanic	.78 [.05, 1.52]	2.11*
Latino	-.19 [-.93, .56]	-0.50
East Asian	-.13 [-.50, .25]	-0.66
South Asian	.43 [-.09, .96]	1.63
Hawaiian/Pacific Islander	-.47 [-1.42, .47]	-0.99
Birth control use	.42 [.22, .62]	4.08***
Anti-depressant use	-.22 [-.46, .03]	-1.77

*p <.05, **p <.01, ***p <.001

Supplementary Tables 14-16: Supplementary Analyses with Alternative Explanations: Relationship Quality, Hostility Toward the Partner, and Loneliness

See Supplementary Tables 14-16 for results with the group-mean-centered total time spent co-present when controlling for relationship quality, hostility with the partner, and loneliness, separately.

Supplementary Table 14

Weekly Fluctuations of Total Time Spent Co-Present Predicting CRP, Controlling for Weekly Relationship Quality.

Predictors	*b* [95% CI]	*t*
Time spent co-present	-.0002 [-.0003, -.00002]	-2.23*
Relationship quality	.006 [-.03, .04]	0.38
Biological sex	.34 [.07, .61]	2.51*
Age	-.001 [-.01, .01]	-0.08
BMI	.05 [.02, .08]	3.45***
Anti-inflammatory use	.22 [.06, .38]	2.71**

*p <.05, **p <.01, ***p <.001

Supplementary Table 15

Weekly Fluctuations of Total Time Spent Co-Present Predicting CRP, Controlling for Weekly Hostility Toward Partner.

Predictors	*b* [95% CI]	*t*
Time spent co-present	-.0001 [-.0003, -.00001]	-2.12*
Hostility	-.04 [-.07, -.001]	-2.04*
Biological sex	.33 [.07, .60]	2.48*
Age	.0003 [-.01, .01]	0.04
BMI	.05 [.02, .08]	3.56***
Anti-inflammatory use	.23 [.07, .38]	2.84**

*p <.05, **p <.01, ***p <.001

Supplementary Table 16

Weekly Fluctuations of Total Time Spent Co-Present Predicting CRP, Controlling for Weekly Loneliness.

Predictors	*b* [95% CI]	*t*
Time spent co-present	-.0002 [-.0003, -.00003]	-2.34*
Loneliness	-.06 [-.15, .03]	-1.29
Biological sex	.34 [.07, .61]	2.49*
Age	-.001 [-.01, .01]	-0.09
BMI	.05 [.02, .08]	3.50***
Anti-inflammatory use	.23 [.07, .38]	2.83**

*p <.05, **p <.01, ***p <.001

Supplementary Table 17: Characteristics of Long-Distance Sample

Supplementary Table 17

Characteristics oof Sample Including Participants in Long-Distance Relationships (N = 159).

	M (*SD*)	% (*n*)
Age	24.70 (7.56)	
Biologically Female		84% (135)
BMI	23.27 (3.9)	
Race/Ethnicity[1]		
White/Caucasian		75.2% (121)
Black/African American		9.3% (15)
Hispanic		3.7% (6)
Latino		3.1% (5)
East Asian		8.7% (14)
South Asian		6.2% (10)
Pacific Islander/Native Hawaiian		0.6% (1)
Middle Eastern		0.6% (1)
Southeast Asian		0.6% (1)
Education Level[2]		
High school graduation or equivalent		5.6% (9)
Some college		49.4% (79)
College graduation		30.0% (48)
Professional/post-graduate degree		15.0% (24)

[1]Groups are not mutually exclusive as participants could endorse more than one race/ethnicity.
[2]We note education level may be confounded with age in this sample ($r = .71$, $p < .001$)

Supplementary Table 18: Primary Analyses Including Long-Distance Sample

Although in the main text we present results for participants who reported not being in a long-distance relationship with their partner and/or having a partner who lived locally, being long distance does not mean the participant didn't see their partner in person on any given week of the study. Because it is within the realm of possibility that the couple members saw each other periodically, we tested if time spent co-present were associated with CRP with the full sample, regardless of long-distance relationship status. See Supplementary Table 18 for model results. Conclusions hold.

Supplementary Table 18

Total Time Spent Co-Present Predicting CRP – Full Sample.

Predictors	*b* [95% CI]	*t*
Time spent co-present	-.0001 [-.0002, -.00003]	-2.65**
Biological sex	.26 [.04, .47]	2.34*
Age	-.001 [-.01, .01]	-0.12
BMI	.04 [.02, .07]	4.02***
Anti-inflammatory use	.34 [.22, .46]	5.71***

*p <.05, **p <.01, ***p <.001

Supplementary Table 19: Sensitivity Analysis Including Individuals with High (>10) CRP

Supplementary Table 19 displays main model results, controlling for standard covariates, using time spent co-present to predict the full range of CRP values (including those greater than 10 μg/mL). Of the 298 CRP samples, two were above 10 μg/mL, and measured at 23.21 and 24.80 μg/mL raw, assessed from two different people. These values are 6.17 and 6.62 standard deviations, respectively, above the (raw) mean value of CRP across all time points. Once log-transformed, the outlying values are 2.72 and 2.77 standard deviations, respectively above the log-transformed mean.

Supplementary Table 19

Total Time Spent Co-Present Predicting CRP, Including the Sample Values above 10 µg/Ml.

Predictors	*b* [95% CI]	*t*
Time spent co-present	-.0001 [-.0002, .00002]	-1.64
Biological sex	.35 [.07, .62]	2.51*
Age	.001 [-.01, .02]	0.17
BMI	.04 [.02, .07]	3.12**
Anti-inflammatory use	.30 [.13, .47]	3.50***

*p <.05, **p <.01, ***p <.001

Supplementary Tables 20 and 21: Exploratory Analyses Using Time Spent Co-Sleeping

Our hypotheses focused on total time spent co-present over the course of a day. However, we also collected exploratory estimates of *how* that time was spent. Given prior associations between sleep duration and inflammation (Irwin et al. 2016; Patel et al. 2009), here we took the opportunity to explore whether the primary analysis could be explained solely by the amount of time spent sleeping next to their partner. To measure time spent co-sleeping, participants estimated how much of the *total* time spent with their partner that they reported from the prior 24 hours was spent sleeping next to them (*range*: 0 – 600 minutes; *M* time 1 = 215.4 minutes; *M* time 2 = 239.9 minutes; *M* time 3 = 225.2 minutes). Two reports of time spent co-sleeping were missing from the dataset (*n* = 297).

We present full models controlling for biological sex, age, BMI and anti-inflammatory use in Supplementary Table 20. We then control for the full set of covariates in Supplementary Table 21 (next page). Time spent co-sleeping was not significantly associated with CRP in either model.

Supplementary Table 20

Time Spent Co-Sleeping Predicting CRP.

Predictors	*b* [95% CI]	*t*
Time spent co-sleeping	-.0002 [-.0004, .00002]	-1.79
Biological sex	.34 [.07, .61]	2.50*
Age	..001 [-.01, .02]	0.12
BMI	.05 [.02, .07]	3.31**
Anti-inflammatory use	.21 [.05, .36]	2.56*

*p <.05, **p <.01, ***p <.001

Supplementary Table 21

Time Spent Co-Sleeping Predicting CRP, Controlling for All Covariates.

Predictors	*b* [95% CI]	*t*
Time spent co-sleeping	-.0002 [-.0004, -.00002]	-1.82
Biological sex	.10 [-.16, .36]	0.77
Age	.01 [-.01, .02]	0.91
BMI	.05 [.03, .08]	4.39***
Anti-inflammatory use	.19 [.03, .35]	2.35*
White	.29 [-.09, .67]	1.52
Black	-.30 [-.72, .12]	-1.41
Hispanic	.78 [.04, 1.52]	2.09
Latino	-.15 [-.90, .60]	-0.39
East Asian	-.13 [-.51, .25]	-0.67
South Asian	.43 [-.10, .96]	1.59
Hawaiian/Pacific Islander	-.45 [-1.40, 0.51]	-0.93
Birth control use	.43 [.23, .64]	4.17***
Anti-depressant use	-.20 [-.44, .05]	-1.61

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