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

Tatum A. Jolink [a], Baldwin M. Way [b], Ayana Younge [c], Christopher Oveis [d], Sara B. Algoe [a,*]

[a] Department of Psychology & Neuroscience, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA
[b] Department of Psychology, Institute for Behavioral Medicine Research, The Ohio State University, Columbus, OH, USA
[c] Kenan-Flagler Business School, University of North Carolina at Chapel Hill, Chapel Hill, NC, USA
[d] Rady School of Management, University of California, San Diego, San Diego, CA, USA

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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 relationship quality may not be as robust a predictor 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 h, 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 independent from social relationship quality 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.

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 and 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 and Way, 2019; Uchino et al., 2018), and even loneliness (Hawkley and Cacioppo, 2003) as being associated with inflammation. Critically, 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). Thus, exactly *how* close relationships could impact the immune system requires further investigation. Here, rather than quality, we focused on what we believed 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 were many reasons we focused on physical co-presence. The first three relate to the fact that close relationship partners are a key structural element of humans' everyday lives. First, *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 has tended to focus on distressing moments (Robles and Kiecolt-Glaser, 2003): relatively satisfying

* Corresponding author at: Department of Psychology & Neuroscience, University of North Carolina at Chapel Hill, 235 E. Cameron Ave. CB #2370, Chapel Hill, NC 27599-3270, USA.
E-mail address: algoe@unc.edu (S.B. Algoe).

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relationships are characterized by interactions that are positively-valenced and affectionate or caring, which may be salubrious in their own right (cf. Algoe, 2019). Second, growing evidence suggests that simply being physically co-present with a loved partner reduces the need for vigilance to threats (Coan et al., 2006; Coan et al., 2017) and increases physiological regulation of the endocrine (i.e. hypothalamic–pituitaryadrenal axis or HPA) and autonomic pathways that influence peripheral inflammation (Beckes and Coan, 2011; Bourassa et al., 2019; Coan and Maresh, 2014; Cornelius et al., 2020; Gump et al., 2001; Han et al., 2021; Phillips et al., 2006). 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., Harbert et al., 2020; Lim and 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). In short, in *high-quality* relationships, people tend to simply spend more time with one another in a variety of ways (e.g., Chang et al., 2022), making time spent co-present one logical factor to take seriously as a potential explanatory mechanism linking close relationships and systemic inflammation.

Fourth, in humans, broad-based measures of social *isolation*, which are not specific to what happens within a given relationship but reflect a potential pattern of a lack of contact (that is, *lack* of time spent co-present) with other humans across relationships, have provided indirect evidence that this is a path worth pursuing. Specifically, 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 focused 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 consequential. People are invested in and care about romantic partners (Algoe and Jolink, 2020), 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 a romantic partner, 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; Coan et al., 2017; Han et al., 2021), a romantic partner can represent a source of safety (Campa et al., 2009; Collins and 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 tested the effect of reported time spent co-present with a romantic partner on systemic inflammation, measured using assay of CRP levels in blood, using the strength of a repeated measures design; we sampled both time spent with the partner and CRP three times across four weeks.[1] As an acute phase protein, CRP is synthesized and released in response to pathogens as well as psychological factors (Pepys and Hirschfield, 2003). CRP levels are not static; in studies of inflammatory clinical conditions, such as rheumatoid arthritis, 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. Sampling CRP at 3 time points increased statistical power to test the association using multilevel statistical modeling and provided the opportunity to assess associations between intraindividual deviations in co-presence with CRP.

Regarding the measure of time spent co-present, participants reported time spent in the physical presence of their partner over the 24 h prior to the blood sample collection. We believed a 24-hour recall would be more accurate than estimating time spent throughout the prior 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 h after injection. To assess the relative importance of physical co-presence with the partner, we also ran analyses controlling for weekly relationship satisfaction, hostility toward the partner, and loneliness; in addition to addressing prior findings in the literature on social relationship quality, relationship satisfaction and hostility can be viewed as proxy measures for quality of time spent together. Finally, we tested the reverse-causal explanatory pathway.

1. Methods

1.1. 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 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 but younger than 60, and were excluded if they were pregnant or nursing (currently or within the past six months), or currently had any of the following: arthritis, rheumatoid arthritis or joint problems, an immune disorder that might lead to immunodeficiency such as HIV, an auto-immune disorder, a chronic disease of the endocrine system (e.g., Cushing's Disease), a psychiatric disorder other than depression or anxiety, a diagnosed sleep disorder, or were currently diabetic. That is, participants were *not* recruited from a clinical population and did not have a history of pathologies related to immune dysfunction. Participants were excluded if they were currently or regularly taking anti-inflammatory medication, such as Tylenol, Ibuprofen or low-dose aspirin. They were also excluded if they indicated they had six or more alcoholic drinks on one occasion "twice a week" or more, as well as if they indicated using marijuana "several times a week" or more. Finally, tobacco smokers were excluded from the study.

Based on an administrative error, participants who considered themselves to be in a long distance relationship were admitted into the study. Because study hypotheses about inflammation are contingent upon participants interacting with their partner *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 indicated that they were both *not* in a long distance relationship *and* that their partner lived locally (N = 100). All other responses (N = 59)

[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 tend to be in loving, satisfied romantic relationships. Thus, the sample was expected to meet the threshold of our theoretical assumption.

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).

1.2. Procedure

Eligible participants were scheduled for a set of three in-lab appointments within a month: at study entry (Time 1), two weeks later (Time 2), and again four weeks later (Time 3). Any given participant came at the same time of day and day of the week for all three of their appointments (e.g., Tuesdays at 10am). The primary purpose of the lab visits was to obtain a blood sample to measure systemic inflammation, as indexed by C-reactive protein (CRP). Due to a lack of consistent evidence for diurnal variability in CRP within blood (e.g., Meier-Ewert et al., 2001; Miles et al., 2008; Mills et al., 2009), session times were offered between 8am and 8 pm. Participants attended their lab sessions between Oct 30, 2017 and Dec 3, 2017 or between Nov 13, 2017 and Dec 17, 2017.

At each appointment, the participant was 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), then behavioral and psychological factors of interest for the research questions. This included the key independent measure of how much time the participant spent in the physical presence of their partner in the prior 24 h. The visit typically took 20–30 min. 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 (Algoe, 2022). 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).

1.3. Measures

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

Social quality 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 with sufficient reliability (α time 1 = .91; α time 2 = .82; α time 3 = .89). 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?"; reliability was adequate at each time point (α time 1 = .80; α time 2 = .84; α time 3 = .85). We tested models controlling for these variables. One report 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 over-the-counter (OTC) medicine 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 h?" (O'Connor et al., 2009).[2] No data were missing from any covariate measure except the use of over-the-counter medicine at the second lab visit, of which a response was missing from one report (*n* = 298).

We explored two additional sets of covariates. In the first, we explored covariates of race/ethnicity, contraceptive use, and use of antidepressants. In the second, we explored whether participants exercised the day of the blood collection ("have you done any aerobic exercise today (e.g., jogging, tennis, karate?", *yes* = 1 or *no* = 0) and sleep quality from the night prior to the blood collection ("how well did you sleep last night?" from *extremely poorly* = 1 to *extremely well* = 10).

C-reactive protein. C-reactive protein (CRP) was measured via dried blood spots, a method which has shown excellent correspondence with CRP concentrations assayed via traditional venipuncture (McDade et al., 2004). For collection, the experimenter swabbed the participant's finger with alcohol, then pricked it 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 h, then punched using a 3 mm 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 et al. (2004), a single 3 mm punch was thawed and 200 μL of buffer (phosphate-buffered saline with 0.1 percent Tween 20) was added, followed by overnight (~16 h) incubation at 4 °C while shaking at 60 rpm. The following morning, eluate was diluted 1:10 and two separate 25 μL aliquots (due to experimenter error, one sample was not processed in

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 ($r = 0.71, p < .001$).

[2] Over-the-counter medicines were reported on only 17 of 298 occasions; medications are detailed in SM. Note that participants were screened out for *regular* use of anti-inflammatory medication; this variable was to control for *occasional* use of medication on appointment days.

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 (i.e., 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),[3] resulting in 296 total observations of CRP. As is common with inflammatory markers (Jaremka et al., 2020; Lee and 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 $r = 0.33$, p <.001; Time 2 $r = 0.28$, $p = .006$; Time 3 $r = 0.30$, $p = .002$.

1.4. Data analysis plan

This was 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. Effect sizes (r) for individual coefficients for each time spent or social relationship quality variable presented in main text were calculated based on the method used by Kashdan and Steger (2006): $r = \sqrt{(t\ 2\ /t\ 2 + df)}$. Full model results can be found in SM.

In addition to the 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 and Yanagida, 2020). These three new values reflected the amount of time spent relative to the participant's average across the three measurements, such that positive values reflected having spent *more* time with their partner than the participant's own average and negative values reflected having spent *less* time with their partner than their own average. 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 – predicted CRP; those additional models are reported in the SM.

2. Results

See Table 2 for zero-order correlations of main study variables and covariates.

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

Consistent with our hypotheses, participants who spent more time co-present with their partner in the prior 24 h had lower CRP, b = -0.0001, $r = 0.13$, $p = .043$, CI95% [-0.0003, -0.00001]. The model controlled for standard sociodemographic and health covariates of biological sex, age, BMI, and recent over-the-counter medicine use. Additionally, results remained consistent when also accounting for race and/or ethnicity, anti-depressant use, and birth control use, as well as when controlling for exercise and sleep quality. See SM for full statistical report. See Fig. 1 for a dual axis plot of means at each time point.

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. Participants who spent more time spent co-present with their partner in the prior 24 h, beyond their average across three time points, had significantly lower CRP, b = -0.0002, $r = 0.16$, $p = .029$, CI95% [-0.0003, -0.00002]. Models once again controlled for biological sex, age, BMI, and recent over-the-counter medicine use, and held when also accounting for race and/or ethnicity, anti-depressant use, and birth control use, and additionally when controlling for exercise and sleep quality. 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: CRP did not predict the time spent together in the prior 24 h, accounting for biological sex, age, BMI and over-the-counter medicine use (see SM).

2.2. Addressing social quality 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 social relationship quality alternative explanation. Time spent co-present significantly negatively predicted CRP, b = -0.0001, $r = 0.13$, $p = .04$, CI95% [-0.0003, -0.00001], when controlling for relationship quality that week, $b = 0.01$, $r = 0.03$, $p = .67$, CI95% [-0.02, 0.04]. Time spent co-present was significantly negatively associated with CRP, b = -0.0001, $r = 0.12$, $p = .05$, CI95% [-0.0003, 0.0000001], when controlling for hostility toward the partner that week, b = -0.04, $r = 0.13$, $p = .04$, CI95% = [-0.07, -0.002]. Lastly, time spent co-present was significantly negatively associated with CRP, b = -0.0001, $r = 0.13$, $p = .032$, CI95% [-0.0003, -0.00001], when controlling for loneliness that week, b = -0.06, $r = 0.08$, $p = .20$, CI95% [-0.15, 0.03]. Each model controlled for biological sex, age, BMI and over-the-counter medicine 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 showed 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 toward the partner, or loneliness. Full model results, including standard covariates, can be found in SM.

3. Discussion

The present study examined the question of 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 loved 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 toward the partner, and loneliness – showing that total time spent co-present consistently predicted CRP, regardless of these other factors relating to social relationship quality. 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 one of humans' most important relationships – with a romantic partner – we showed in a fine-grained way that one possible mechanism for effects of

[3] Sensitivity analyses including individuals with high CRP (greater than10 ug/mL) can be found in Supplemental Material.

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	0.82***	–							
3. CRP Time 3	0.82***	0.82***	–						
4. Time spent T1	0.01	0.04	0.04	–					
5. Time spent T2	-0.02	-0.06	-0.07	0.63***	–				
6. Time spent T3	0.02	0.02	-0.07	0.52***	0.54***	–			
7. Biological sex	0.20*	0.17	0.21*	0.02	-0.07	-0.05	–		
8. Age	0.12	0.14	0.10	0.25*	0.17	0.19	0.06	–	
9. BMI	0.33***	0.28**	0.30**	0.04	0.04	-0.08	-0.07	0.39***	–

*p <.05, **p <.01, ***p <.001.
Note: Time spent are raw values, in minutes. CRP are log-transformed. T = time point.

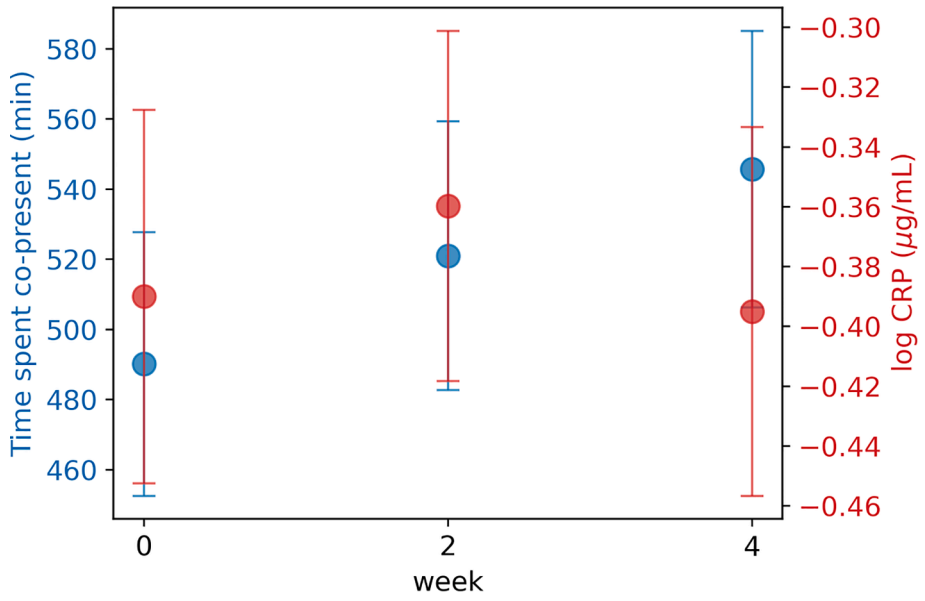

Fig. 1. *Note*. Dual-axis plot depicting mean levels of raw time spent co-present (in minutes) and log-transformed CRP values at each time point. Error bars represent the unbiased standard error of the mean.

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 and Kirkpatrick, 1996), here, we do not make the assumption that stress-buffering was 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 and Pressman, 2006; Folkman and Moskowitz, 2000; Pressman et al., 2019), physical affection (Holt-Lunstad et al., 2008; Thomas and 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 these findings were correlational, so although we hypothesize causality, we await stronger tests of the causal hypothesis. Further, theory and evidence could suggest the reverse direction explanation. For example, early theory suggested that the release of pro-inflammatory cytokines was associated with the prototypical "sickness behavior" of social withdrawal, and some human studies provided initial support for that using a broad array of relationship types (Eisenberger et al., 2009; Eisenberger et al., 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 and Inagaki, 2021), with the potential for people to want to *approach* close partners, such as romantic partners. Indeed, heightened inflammation has been associated with or caused 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, the 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 relationships and inflammation (Holt-

Lunstad et al. 2010; Smith et al. 2020; Uchino et al 2018), yet stand in contrast to the prior focus on social relationship *quality* factors. Romantic relationship quality and loneliness were not associated with CRP in our sample, despite associations with inflammation in the prior literature (Bajaj et al., 2016; 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 has shown hostility and strain in close relationships to be associated with greater inflammation (Brooks et al., 2014; Gouin et al., 2009; Kiecolt-Glaser et al., 2005; Kiecolt-Glaser et al., 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 has also raised questions about the strength of associations 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 and Hayes, 2001; John and Gross, 2004; Overall and McNulty, 2017; Torre and 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 couples when hostility is at its nadir, as these insights might guide future predictions regarding inflammation.

We also draw attention to five 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 and Coan, 2011), is that even poor relationships still offer slightly more benefit than being alone. Alternatively, relationships with substantially greater stress and negative affect may produce the opposite to what was found here. That question needs to be tested empirically. Second, a related question is whether there are individual differences in the way people view their experiences with their partners, or even whether actual variability in the quality of the time spent together across different days, may moderate the association between time spent and CRP specifically, or another marker of inflammation. Third, 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., 2022). That said, there are likely other objective measures of time spent in physical co-presence that would help to augment future study designs. Fourth, inflammatory markers can be influenced by multiple factors. Though the effects held when adjusting for self-reported sleep and exercise, the measurement of these variables would also be enhanced by using objective measures. Similarly, we did not measure potential dietary contributions to these shifts over time (Shivappa et al., 2014). Fifth, these effects may not be unique to CRP, so future work should examine physical co-presence and other markers of inflammation to provide greater insight into the potential cellular pathways contributing to this effect as well as ensure that the effects on CRP are indeed due to peripheral inflammation and not another biological process (Del Giudice and Gangestad, 2018).

In conclusion, 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 and Keller, 2000; Kiecolt-Glaser et al., 2010; Ridker, 2009). We sampled CRP on three different days across time, and found evidence suggesting merely being together with a romantic partner was 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.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

Data will be made available on request at this link: https://doi.org/10.15139/S3/SHX8HC.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.bbi.2022.09.007.

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