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Full-length Article

Parental support buffers the association of depressive symptoms with cortisol and C-reactive protein during adolescence [☆]Shu-Sha Angie Guan ^{a,*}, Julienne E. Bower ^b, David M. Almeida ^c, Steven W. Cole ^b, Ronald E. Dahl ^d, Michael R. Irwin ^f, Teresa E. Seeman ^b, Thomas McDade ^e, Andrew J. Fuligni ^f^a California State University, Northridge, United States^b University of California, Los Angeles, United States^c Pennsylvania State University, United States^d University of California, Berkeley, United States^e Northwestern University, United States^f Cousins Center for Psychoneuroimmunology, Semel Institute for Neuroscience, University of California, Los Angeles, United States

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ABSTRACT

Social experiences can affect the relationship between depression and physical health. The current study examined how social support from parents and friends may moderate the association of depressive symptoms with hypothalamic-pituitary-adrenal (HPA) axis activity and C-reactive protein among adolescents ($N = 316$, $M_{age} = 16.40$, $SD = .74$; 57% female) from diverse ethnic backgrounds (23.1% Asian, 29.1% European, 41.8% Latino, and 6.0% other backgrounds). Results indicated that parent support, but not friend support, moderated the link between depressive symptoms and both total daily cortisol output (a measure HPA activity) and C-reactive protein (a marker of inflammation). These patterns did not differ by ethnicity. Overall, the study highlights the continued, and perhaps accumulated, importance of parents during adolescence despite increasing needs for autonomy from and exploration outside of the family unit.

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Introduction

Major depression is one of the most common psychiatric disorders afflicting adolescents (Kessler et al., 2012; Lewinsohn et al., 1993). First depressive onset is most likely to occur during this developmental period and lifetime rates of depression rise from childhood to comparable adult rates during adolescence (Avenevoli et al., 2008; Kessler et al., 1994; Lewinsohn et al., 1993). Depression during adulthood has been associated with poor physical health (e.g., Ferichs et al., 1982). Protective mechanisms

such as social support are important to examine during this period of emergent depression risk given that adolescence often sets the stage for later adult health. Additionally, social support from different sources may confer different benefits during adolescence, a period marked by 'social re-orientation' (Nelson et al., 2005). The current study examined how positive social experiences from parents and friends may differentially moderate the association of depressive symptoms with biological markers of physical health in adolescents from diverse backgrounds. Specifically, this study examined how social support may moderate the link between depressive symptoms and cortisol, the hormone end-product of the hypothalamic-pituitary-adrenal (HPA) axis, and C-reactive protein, a marker of inflammation linked to cardiovascular disease. Both are indices associated with physical health outcomes (Koenig et al., 1999; Matthews et al., 2006). These physiological systems are also believed to be responsive to psychosocial experiences, particularly during adolescence.

Depression during adolescence

The development of affective disorders during adolescence may be a product of neurophysiological changes in social-affective

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processing during puberty (Byrne et al., 2015; Crone and Dahl, 2012; Nelson et al., 2005). Adolescents show heightened emotional responsiveness and physiological reactivity to social stimuli and experiences compared to adults (Monk et al., 2003; Sumter et al., 2010). Although negative interpersonal experiences in adolescence have been associated with depressive symptoms (La Greca and Harrison, 2005), positive social experiences such as social support may be protective (Lewinsohn et al., 1994; Stice et al., 2004; Windle, 1992).

Depression and the HPA axis

It is believed that neurobiological pathways may underlie the processes through which social experiences contribute to depression (Kendler et al., 1999; Müller and Schwarz, 2007). Social stressors that activate the HPA axis, leading to the release of glucocorticoids, have been associated with the development of depressive behaviors in animal models (Bodnoff et al., 1995). A recent meta-analysis of human data suggests that elevated corticotropin-releasing hormone and basal cortisol levels in the morning, noon and night are hallmarks of major depression among adults (Murri et al., 2014).

Among adolescents, pubertal onset may create a window of vulnerability and opportunity at the level of interactions between regulatory systems (e.g., stress regulation and affect dysregulation; Colich et al., 2015; Dahl and Gunnar, 2009). Adolescents who exhibit higher morning cortisol levels, greater rises in morning cortisol (i.e., cortisol awakening response [CAR]) and less efficient down-regulation of cortisol across the day (i.e., flatter diurnal cortisol slopes [DCS]) tend to be at greater risk for having depression (Adam et al., 2010; Doane et al., 2013; Owens et al., 2014). The current study examined how social factors may moderate this link between depressive symptoms and HPA activity, especially during a transitional period of biological and social flux (Crone and Dahl, 2012).

Depression and inflammation

Depression also is often coupled with inflammation. Depressed adults exhibit higher levels of pro-inflammatory biomarkers like C-reactive protein (CRP) and cytokines (e.g., IFN- α , IL-2) (for reviews see, Irwin and Miller, 2007; Raison et al., 2006). Direct administration of pro-inflammatory cytokines in healthy young adults and older adult patients undergoing immunotherapy can also induce sickness behaviors characteristic of depression such as sad mood, fatigue, sleep disturbance, attention/memory impairment and social withdrawal (Capuron et al., 2002; Reichenberg et al., 2001; Strike et al., 2004; Wright et al., 2005; Yirmiya et al., 2000).

Dysregulation of the HPA axis and immune system can interact with social experiences, strengthening a risk pathway over time. Although glucocorticoids may have immunosuppressive effects, feedback loops between the neuroendocrine and immune systems may become impaired within certain conditions such as chronic stress (Irwin and Miller, 2007; Miller et al., 2013; Pace et al., 2007; Raison and Miller, 2003; Slavich and Irwin, 2014). That is, chronic HPA activation may result in impaired glucocorticoid-mediated inhibition of pro-inflammatory immune responses. This glucocorticoid resistance is one pathway that can lead to chronic inflammation and the persistence of depression-like symptoms. In addition to affecting HPA activity, growing evidence suggests that hormonal changes during puberty may be associated with increased risk for depression and inflammation, especially among chronically distressed youth (Byrne et al., 2015; Miller and Cole, 2012; Mitchell and Goldstein, 2014).

Social support as a buffer

Social support may be a protective coping mechanism that reduces the negative effects of stressful experiences on physiological processes and health outcomes in adults (Cohen and Wills, 1985; Seeman, 1996). Support may affect mental and physical health through dampening psychological and physiological reactivity to threatening or challenging events (Cohen and Wills, 1985; Seeman and McEwen, 1996; Uchino et al., 1996). Work examining the potential neurocognitive mechanisms suggest that greater social support may diminish activity in neural regions associated with pain, fear, distress and social separation, that then reduce cortisol and inflammatory reactivity (Eisenberger, 2013; Eisenberger and Cole, 2012; Eisenberger et al., 2007). These studies suggest that positive social experiences that signal social inclusion can alter perceptions of challenge and subsequent physiological responses.

Among older adults, high levels of social support may moderate the relationship between inflammation and depression (Capuron et al., 2004). However, not all studies have found a significant main or moderating effect of social support to physical health markers (McDade et al., 2006; Reblin and Uchino, 2008). Reblin and Uchino (2008) suggest that the lack of consistency may be due to differences in support measures across studies (e.g., in a single context or source, perceived or received). For example, perceptions of available support (perceived support) can be influenced by early family environments and, therefore, is oftentimes stable and related to personality factors (Uchino, 2009). Received support, on the other hand, may be more context-dependent and can co-occur with stressful life circumstances. That is, those who are more stressed may seek out greater support and close social network members may also begin to initiate support provision in times of need.

Additionally, the particular characteristics of sample populations (e.g., older adults, clinical samples) may shape the effects of social support in moderating risk pathways. Indeed, adult disease pathways that link depression and physiological processes themselves seem to vary across the lifespan (Andreoli et al., 1993; Bilbo and Schwarz, 2012; Bodnoff et al., 1995; Irwin and Miller, 2007; Murri et al., 2014). The impaired feedback loop in the neuroendocrine, central nervous and immune systems may begin to emerge and become strengthened during developmental periods such as adolescence, in which physiological systems are calibrating for what may be most adaptive in a particular context (Del Giudice et al., 2011; Low et al., 2013; Miller et al., 2013; Murri et al., 2014; Raison and Miller, 2003). This may be especially true for those with higher life stress and reduced capacity for coping. Despite the potential differences, little research has examined these links among adolescents.

In addition to biological changes, dramatic social changes occur during this period. Adolescence is often marked by growing social networks outside of the family unit. Given increased mobility and coupled with desires for autonomy and egalitarianism, adolescents can begin to exhibit a growing reliance on peers and increased conflict with parents (Brown, 1990; Erikson, 1968; Fuligni and Eccles, 1993; Furman and Buhrmester, 1992). The changes are often reflected in reported levels of social support (Furman and Buhrmester, 1992; Scholte et al., 2001). Yet few studies have compared important support sources during transitional developmental periods.

The current study

Overall, there appears to be a bidirectional, causal relationship of depression to HPA dysregulation and inflammation that gets

strengthened over time. Positive social experiences, such as social support, may contribute to or disrupt this biological encoding. It is particularly important to examine factors that may moderate these pathways during adolescence given the heightened sensitivity of stress-response systems like the HPA axis and emergence of affective disorders during this developmental period. Despite this, little is known about how various social resources moderate the links of depression with HPA activity and inflammation among adolescents. To address this gap, the current study examined how social support from parents and friends may moderate the associations of depressive symptoms with HPA activity and inflammation among adolescents from diverse ethnic backgrounds. Specifically, this study aimed to examine (a) the link between depressive symptoms and daily cortisol output, (b) the link between depressive symptoms and CRP, and (c) the moderation of these relations by perceived social support from parents and friends.

Method

Participants

A total of 316 adolescents ($M_{age} = 16.40$, $SD = .74$; 57% female) from Asian (23.1%), European (29.1%), Latin American (41.8%) and other ethnic (6.0%) backgrounds were recruited through home mailings and oral presentations made in 10th and 11th grade classrooms in four high schools in the Los Angeles area. Adolescents' primary caregiver (89.5% biological mothers, 2.25% stepmother/adoptive mother, and 8.25% other) reported their highest level of education from 1 = *some elementary school* to 11 = *graduated from medical, law, or graduate school* and the highest education level of the adolescent's second parent. Parent education was created by taking the mean of the standardized values of mother and father education ($M = 7.19$, $SD = 1.81$). Parents' average level of education was between trade or vocational school and some college. One-way ANOVAs with Bonferroni comparisons indicated that individuals from Asian and Latin American families reported lower parent education levels than those from European and other backgrounds, $F(3, 309) = 16.08$, $p < .001$.

Procedures

Students who indicated interest in response to the mailing or school presentations were contacted and given more details about the study. Those who provided verbal parental consent were scheduled for a visit either at the participants' homes or at a local field research center. During this initial visit, adolescents provided anthropometric measures and completed a computer-assisted personal interview that included standard psychosocial measures and took approximately 1 h to complete. Translators fluent in Spanish and Chinese (Mandarin and Cantonese) were made available. Upon completion of the survey, finger-prick blood samples for CRP analysis were obtained on the same day. Participants were given at-home saliva kits and were instructed to use the Salivette cotton swabs (Sarstedt, Numbrecht, Germany) at five time points across the next three consecutive days: (1) at wake, (2) 15 min after wake, (3) 30 min after wake, (4) before dinner, and (5) before bed. Participants were instructed to take their morning samples before brushing their teeth, drinking or eating anything. A stamping booklet and electronic time stamper (Dymo Corporation, Stamford, Connecticut) that imprinted the date and time was provided so that participants could record daily saliva collection and aid in compliance. They also reported wake times in daily diaries for each of the three days. Participants were sent text message reminders on their cellphones before each daily diary entry and cortisol sample. Adolescents were paid \$50.00 for their participation in the study.

Families were also mailed free movie tickets along with health reports that included information such as their body mass index (BMI).

Measures

Depressive symptoms

Symptoms of depression were assessed through a 20-item scale from the Center for Epidemiologic Studies Depression Scale (CES-D, Radloff, 1977). Participants were asked to report on how frequently (0 = *rarely* to 3 = *most of the time*) they felt a certain way (e.g., "I was bothered by things that usually don't bother me," "I felt lonely," "I felt that people disliked me") in the past month. Items were summed. Although a clinical cutoff of 16 has been used for adults, a cutoff of 28 may be more appropriate for adolescents (Radloff, 1991). Approximately 15.2% of participants scored 28 or above. Cronbach's α was .80.

Social support

Adapted from Furman and Buhrmester (1985, 2009), the measure asked participants to report how frequently in the past 12 months parents and friends provided informational, instrumental, and emotional support (i.e., *How often [your parents/friends] given you advice about your future career plans? How often have [your parents/friends] given you assistance [money, transportation, etc.]? How often have [your parents/friends] expressed interest, respect, or care in you? and How often have the [your parents/friends] helped cheer you up when you were feeling down or upset?*) on a scale from 1 (*almost never*) to 5 (*almost always*). Cronbach's alphas (α s) for parent and peer support were .74 and .68, respectively.

Body mass index

Body mass index (BMI) controlled for abdominal fat, a prime source of inflammation. Interviewers assessed height and weight using a stadiometer and scale. BMI was calculated based on the Center for Disease Control (CDC) height and weight formula where weight in pounds was divided by squared height in inches and multiplied by 703.

CRP

Dried blood spots (DBS) were obtained the same day as anthropometric and psychosocial survey measures through a minimally-invasive procedure in which the index finger is pricked with a lancet by the participants themselves or by an interviewer. Ten blood drops were allowed to fall onto filter paper without touching the paper. After collection, the samples were covered, dried overnight, and frozen in airtight containers at -80°C . CRP concentrations were assessed in the Laboratory for Human Biology Research at Northwestern University using a modified high-sensitivity enzyme immunoassay protocol with a lower detection limit of 0.028 mg/L (McDade et al., 2004). This assay was previously developed for DBS use and validated to produce results comparable to serum-based clinical methods. For each sample, one 3.2 mm disc of blood was punched out, eluted overnight at 4°C in 250 μL assay buffer, and then transferred to 100 μL of eluate to the assay plate. To minimize between-assay variation, all samples were analyzed using a single lot of capture antibody, detection antibody, and calibration material. All samples were run in duplicate and intra- and inter-assay-coefficients of variation were $<6.4\%$ and $<9.3\%$ respectively. Dried blood spots provide whole blood CRP concentrations that differ from values in serum due to the presence of lysed erythrocytes and associated matrix effects, therefore we generated a conversion formula by analyzing $n = 51$ matched DBS and serum samples, collected for a prior assay validation study as recommended by previous research (McDade, 2014). DBS samples were analyzed using the same procedures, lot number and reagents, and

technician as applied to the study DBS samples. Serum samples were analyzed for high sensitivity CRP in a high throughput clinical laboratory, on the Beckman Coulter Synchron DXC platform. The correlation between the DBS and serum values was high ($r = .98$) and the resulting Deming regression conversion formula was as follows: serum (mg/L) = $1.84 \times$ DBS (mg/L). All analyses in the present paper used this formula to generate serum-equivalent values to facilitate comparisons with clinically relevant cut-off values (Pearson et al., 2003). The lower limit of detection for the assay 0.06 mg/L (serum equivalent).

Eleven participants had levels of CRP >10 mg/L, which is the recommended cut-off value for identifying acute elevations in CRP that do not represent chronic levels of inflammation (Pearson et al., 2003). These individuals were excluded from the analyses though inclusion of these participants in final models did not change results. Additionally, although the majority of participants provided blood drops (98.1%), six adolescents did not or could not provide blood samples and are not included in analyses. Finally, CRP values were log transformed to normalize data in final analyses.

Cortisol

Approximately 97.5% of participants ($n = 308$) provided at least one saliva sample, 96.2% ($n = 304$) provided saliva samples for at least one day, and 86.1% ($n = 272$) provided all five samples on all three days. Samples were removed from analyses if cortisol values >60 nmol/L ($n = 2$) or if they were paired with noncompliant sampling time recording (e.g., reporting the same sampling time for all five samples within the same day, $n = 2$) as in Stawski et al. (2013). Saliva samples were frozen and stored at -20°C until assay. After thawing, Salivettes were centrifuged at 3000 rpm for 5 min and salivary concentrations of cortisol were measured using a commercially available chemiluminescence-immunoassay with high sensitivity (IBL International, Hamburg, Germany). The intra- and inter-assay coefficients for cortisol were below 8%. Cortisol values were log transformed before analyses to normalize the data. Sampling times from the stamping booklet were converted into number of hours past midnight ($M_{\text{wake}} = 7.80$, $SD = 1.47$; $M_{15\text{post-wake}} = 8.06$, $SD = 1.47$; $M_{30\text{post-wake}} = 8.35$, $SD = 1.45$; $M_{\text{dinner}} = 19.04$, $SD = 1.42$; and $M_{\text{bedtime}} = 22.84$, $SD = 1.26$).

Daily cortisol output was assessed by calculating the area under the curve (AUC) relative to ground using all five log-transformed cortisol values (Pruessner et al., 2003). Average cortisol awakening response (CAR), that represents the normative rise in cortisol levels upon awakening, and average diurnal cortisol slope (DCS), that represents the decline in cortisol levels across the day, were also calculated (Stawski et al., 2013). The CAR was calculated by subtracting peak (30 min after wake) from wake values and dividing by the number of hours separating the two samples. The resulting values are positive, reflecting the rising rate of cortisol per hour in the morning. The DCS was calculated by subtracting bedtime from peak values and dividing by the number of hours between samples. The resulting values are negative, reflecting the rate of cortisol decline after the morning peak. Participants missing a relevant cortisol value or sampling time were also missing an AUC, CAR or DCS value for that particular day. Averaging these cortisol indices across the three sampling days increased the likelihood of obtaining at least one estimate of these parameters for each individual (AUC, $n = 285$; CAR, $n = 292$; DCS, $n = 288$). Having sufficient values for one day was enough to be included in the analyses.

Average wake times in the 3 sample days may affect cortisol and were controlled for in cortisol AUC and slope analyses. Sampling times were controlled for in analyses of wake and bedtime cortisol levels. Additionally, a dummy-coded flag variable was created to indicate if a participant was noncompliant in providing samples on any of the 3 sampling days. Specifically, noncompliance

was defined as reporting less than exactly 15 min between sample 1 and 2 (.039% of samples), >20 min between sample 1 and 2 (.010%), <15 min between sample 1 and 3 (.002%), and >60 min between sample 1 and 3 (.002%) used to estimate the CAR. We used a conservative control in which individual participants were assigned a code of 1 if they had a non-compliant sample for any of the specified flags on any of the three sampling days. This non-compliance dummy-code was included as a control in models with cortisol. The inclusion of the noncompliance control did not change the results and was subsequently removed from the final models.

Results

Table 1 shows that the sample was relatively healthy with low depressive symptoms and high average levels of parent and friend support. When DBS CRP values were converted to comparable serum levels (McDade et al., 2004), the majority of participants (69.6%) were in the clinically-defined low-risk range for serum CRP (<1 mg/L), 16.5% were borderline (1–3 mg/L), 8.5% were moderately high-risk (3.01–10 mg/L) and 3.5% were markedly high-risk (>10 mg/L). These values are comparable to other samples of adolescents (Ford et al., 2003; Lambert et al., 2004).

One-way ANOVAs with Bonferroni comparisons indicated adolescents from Latin American backgrounds had higher BMI than adolescents from Asian and European backgrounds, $F(3, 309) = 6.07$, $p < .001$. Adolescents from Asian backgrounds reported lower levels of parent support compared to adolescents from European and Latin American backgrounds, $F(3, 209) = 4.07$, $p = .007$. Females reported higher levels of depressive symptoms ($M = 17.21$, $SD = 10.73$ vs. $M = 13.70$, $SD = 9.91$) and friend support ($M = 3.72$, $SD = .72$ vs. $M = 3.54$, $SD = .79$) compared to males, $ps < .05$. They also had higher levels of cortisol AUC ($M = 27.16$, $SD = 7.49$ vs. $M = 23.87$, $SD = 7.62$), cortisol levels at waking ($M = 2.77$, $SD = .45$ vs. $M = 2.63$, $SD = .52$), and cortisol at bedtime ($M = .63$, $SD = .68$ vs. $M = .39$, $SD = .66$) than males, $ps < .05$ respectively.

Bivariate correlations in Table 1 indicated that depressive symptoms were positively correlated with AUC ($r = .19$) and CAR ($r = .14$). Parent support and friend support were not associated with CRP ($rs = .05$, $.04$, respectively) but friend support was positively correlated with AUC ($r = .12$). Notably, CRP was not significantly related to any HPA outcome (AUC, wake, bedtime, CAR, DCS; $rs = -.06$ to $.02$).

To examine the moderating role of social support in the associations of depressive symptoms with AUC and CRP, a series of hierarchical regressions were estimated. In Step 1, sociodemographics, BMI, depressive symptoms, parent or peer support, and other controls were entered. In Step 2, the interaction between parent or friend support and depressive symptoms was entered. Constituent variables of the interaction terms were standardized into z-scores before they were entered into regression models for interpretation of the intercept and to reduce multicollinearity with interaction terms.

Predicting cortisol

Fig. 1 graphically represents the role of parental support over the entire diurnal rhythm. It shows the average cortisol levels of participants with low levels of parent support and depressive symptoms above and below the adolescent 28-cutoff across the sampling times in a day. Raw cortisol values were used for ease of interpretation and averages controlled for covariates in the final models (age, gender, ethnicity, parent education, BMI, and sampling time).

As shown in Table 2, females ($b = 1.65$, $SE = .47$) and individuals who reported higher depressive symptoms ($b = 1.08$, $SE = .48$)

Table 1
Descriptive data and correlations for study variables.

Variable	M	SD	2	3	4	5	6	7	8	9	10	11
1. Parent Education	7.19	1.81	-.11	-.03	.03	.03	-.17**	.04	-.07	-.04	.04	-.06
2. Body Mass Index (BMI)	23.16	5.01	-	.02	.00	.01	.45**	-.03	-.02	-.02	-.04	.00
3. Depressive Symptoms (0–60)	15.70	10.51		-	-.23**	-.06	.02	.19**	-.05	.09	.14*	-.02
4. Parent Support (1–5)	4.32	.70			-	.24**	.05	.02	.11	.06	-.05	-.01
5. Friend Support (1–5)	3.64	.75				-	.04	.12*	-.01	.08	.05	.07
6. Serum-equivalent CRP (log)	-.77	1.38					-	-.06	-.03	.06	-.06	.02
7. Cortisol AUC	25.78	7.70						-	.17**	.44**	.40**	.17**
8. Wake Cortisol	2.71	.49							-	.14*	-.47**	-.15*
9. Bedtime Cortisol	.53	.68								-	-.01	.62**
10. CAR	.46	1.10									-	-.25**
11. DCS	-.17	.06										-

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

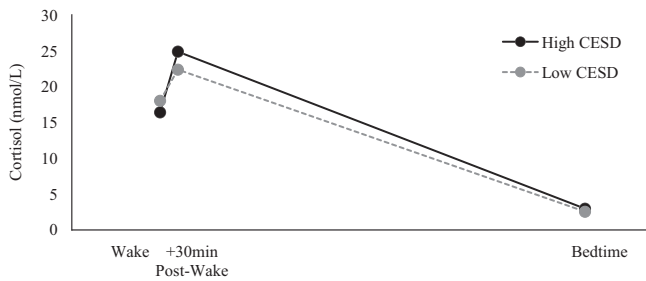


Fig. 1. Average raw cortisol levels for participants who reported low parent support and depressive symptoms above (High CESD) and below (Low CESD) the adolescent CESD cutoff score of 28 across the sampling times in a day. All covariates from the final models in Table 2 are controlled for in the average cortisol values shown in the figure.

exhibited higher AUC levels. As shown in column 2, parent support interacted with depressive symptoms to predict AUC ($b = -.97$, $SE = .45$). Given the interaction, parent support was split at the standardized mean ($z = 0$) and follow-up regressions were estimated to examine the simple-effect associations between depressive symptoms and AUC for those high and low in parent support. Fig. 2 shows that for individuals who reported low levels of parent support, higher levels of depressive symptoms were significantly associated with higher daily total cortisol output ($b = 2.37$, $SE = .72$). The association between depressive symptoms and AUC was not apparent for individuals with high levels of

parent support ($b = .26$, $SE = .63$). In addition to this comparison of simple slopes for these groups of participants, analyses identifying regions of significance more precisely (Preacher et al., 2006) showed that slopes were non-significant between centered parental support values of $z = .12$ – 14.72 . Simple slopes are significant outside of this region. Approximately 39.3% of participants had standardized parental support scores below and 60.7% had values above .12. Fig. 3a shows regions of significant and non-significant simple slopes of depressive symptoms to AUC at conditional values of parent support. Higher friend support was associated with higher AUC ($b = .92$, $SE = .44$), but friend support did not

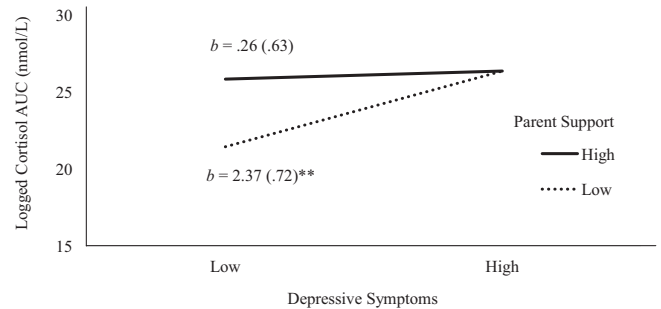


Fig. 2. Association between depressive symptoms and AUC as a function of high and low parental support. Predicted values represented in the figure are based upon the final models in Table 2 and include all covariates.

Table 2
Stepwise hierarchical regression models predicting cortisol area under the curve from depressive symptoms, parent support and friend support.

	Parent Support		Friend Support	
	Step 1 <i>b</i> (<i>SE</i>)	Step 2 <i>b</i> (<i>SE</i>)	Step 1 <i>b</i> (<i>SE</i>)	Step 2 <i>b</i> (<i>SE</i>)
Intercept	25.56 (0.84)**	25.31 (0.84)**	25.48 (0.83)**	25.46 (0.83)**
Age	-.37 (0.46)	-.36 (0.46)	-.42 (0.46)	-.40 (0.46)
Gender	1.59 (0.47)**	1.65 (0.47)**	1.54 (0.46)**	1.65 (0.47)**
Latino	.06 (1.13)	.16 (1.13)	.15 (1.13)	.14 (1.13)
Asian	.30 (1.31)	.32 (1.30)	.36 (1.28)	.44 (1.28)
Other	-2.33 (2.08)	-2.41 (2.06)	-2.19 (2.06)	-2.13 (2.06)
Parent Education	.41 (0.48)	.45 (0.48)	.38 (0.48)	.40 (0.48)
BMI	-.31 (0.46)	-.25 (0.45)	-.35 (0.45)	-.29 (0.46)
Depressive Symptoms	1.24 (0.48)*	1.10 (0.48)*	1.23 (0.46)*	1.20 (0.47)*
Support	.25 (0.47)	.34 (0.47)	.92 (0.44)*	.87 (0.44)
Average Wake Time	-1.62 (0.47)**	-1.66 (0.47)**	-1.64 (0.47)**	-1.68 (0.47)**
Depressive Symptoms × Support		-.97 (0.45)*		.45 (0.43)

Note. Cortisol values were log-transformed before analyses. Gender was effect-coded such that males were coded -1 and females coded 1. European Americans were coded as the reference group for ethnicity. All other continuous predictors were mean-centered as z-scores.

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

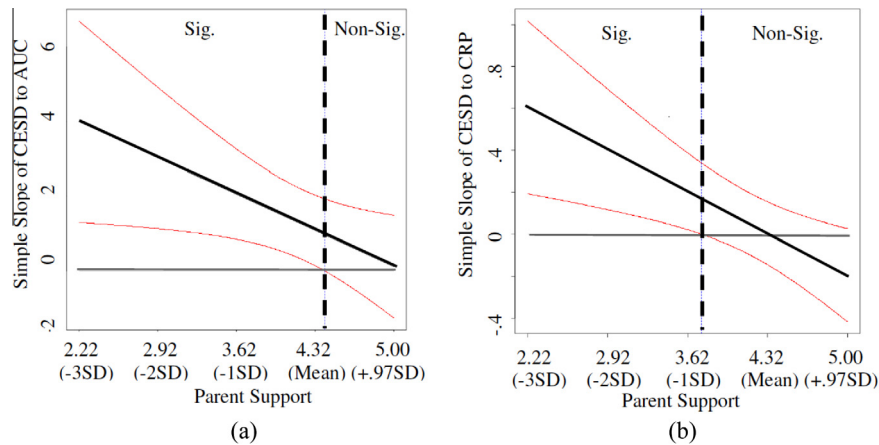


Fig. 3. Graphs show simple slopes of depressive symptoms (CESD) to outcomes (y-axis) at continuous conditional values of parent support (x-axis) in black solid lines for (a) AUC and (b) serum-equivalent CRP. Confidence intervals around values are indicated by the red lines. Dashed black lines indicate separation of simple slope regions of significance from regions of non-significance at standardized and non-standardized values of parent support. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Table 3

Stepwise hierarchical regression models predicting cortisol samples and slopes from depressive symptoms, parent support and friend support.

	Waking		Bedtime		CAR		DCS	
	Parent	Friend	Parent	Friend	Parent	Friend	Parent	Friend
Intercept	2.77 (.05)**	2.76 (.05)**	.65 (.08)**	.64 (.08)**	.43 (.12)**	.47 (.12)**	-.16 (.01)**	-.17 (.01)**
Age	-.03 (.03)	-.03 (.03)	.02 (.04)	.02 (.04)	-.09 (.07)	-.09 (.07)	.01 (.00)	.01 (.00)
Gender	.08 (.03)*	.09 (.03)*	.12 (.04)*	.13 (.04)*	.10 (.07)	.08 (.07)	.00 (.00)	.00 (.00)
Latino	.00 (.07)	.00 (.07)	-.20 (.10)	-.20 (.10)	-.09 (.16)	-.10 (.17)	-.01 (.01)	-.01 (.01)
Asian	-.15 (.08)	-.17 (.08)*	-.15 (.12)	-.15 (.12)	.10 (.19)	.13 (.19)	.00 (.01)	.00 (.01)
Other	-.20 (.13)	-.19 (.13)	-.35 (.18)	-.33 (.18)	.05 (.30)	.07 (.31)	-.02 (.02)	-.02 (.02)
Parent Education	-.04 (.03)	-.04 (.03)	-.04 (.04)	-.03 (.04)	.06 (.07)	.05 (.07)	-.01 (.00)	-.01 (.00)
BMI	-.04 (.03)	-.04 (.03)	-.03 (.04)	-.03 (.04)	-.01 (.07)	-.02 (.07)	.00 (.00)	.00 (.00)
Depressive Symptoms	-.02 (.03)	-.04 (.03)	.05 (.04)	.04 (.04)	.09 (.07)	.13 (.07)	.00 (.00)	.00 (.00)
Average Sampling/Wake Time	-.04 (.03)	-.05 (.03)	.05 (.04)	.04 (.04)	-.11 (.07)	-.09 (.07)	-.01 (.00)	-.01 (.00)
Support	.03 (.03)	-.01 (.03)	.04 (.04)	.04 (.04)	.00 (.07)	.06 (.07)	.00 (.00)	.00 (.00)
Depressive Symptoms × Support	.02 (.03)	.00 (.03)	.02 (.04)	.04 (.04)	-.18 (.06)**	.01 (.06)	.01 (.00)**	.01 (.00)

Note. Step 2 results shown. Cortisol outcomes are averages and from logged cortisol values. Each support source was modeled separately. Waking = cortisol level at wake sample. Before bed = cortisol level at before bedtime sample. CAR = cortisol awakening response. DCS = diurnal cortisol slope. Sample time was controlled in analyses of waking and bedtime cortisol levels analyses. Wake time was controlled in models of CAR and DCS. Support and depressive symptoms were mean-centered as z-scores.

* $p < .05$.

** $p < .01$.

significantly moderate the association between depressive symptoms and AUC ($b = .45$, $SE = .43$). Follow-up three-way interactions by ethnicity and gender were not significant.

In order to examine elements of the diurnal rhythm of cortisol that contribute to AUC, similar regressions were modeled to predict waking cortisol, bedtime cortisol, CAR, and DCS. As shown in Table 3, parent support did not moderate the association between depressive symptoms and single-sample cortisol levels (i.e., waking [$b = .02$, $SE = .03$], bedtime [$b = .02$, $SE = .04$]), but did significantly moderate the relationship between depressive symptoms and cortisol slope values (i.e., CAR [$b = -.18$, $SE = .06$], DCS [$b = .01$, $SE = .00$]). The sample was split at the standardized mean and follow-up regressions were estimated to examine the simple-effect associations between depressive symptoms with CAR and DCS for those high and low in parent support. Results indicated that among adolescents who reported low levels of parent support, higher depressive symptoms were associated with a steeper CAR ($b = .37$, $SE = .12$, $p = .002$). There was no association between depressive symptoms and CAR among those with high levels of parental support ($b = -.07$, $SE = .08$, $p = .383$). Analyses identifying regions of significance showed that slopes were non-significant between centered parental support values of $z = -.25$ to 2.60. Approximately 26.58% of participants had standardized

parental support levels below $-.25$. Depressive symptoms were not associated with a steeper DCS for those who were higher or lower than average in parent support ($bs = .01$, $-.01$, $SEs = .01$, $ps = .215$, $.267$, respectively), even though the slopes were in opposite directions and the original interaction term was significant. Analyses identifying regions of significance showed that slopes were non-significant between centered parental support values of $z = -1.10$ to 1.49.

Predicting C-reactive protein

As shown in Table 4, older adolescents and those with higher BMI exhibited higher CRP levels ($bs = .27$ – $.62$, $SEs = .07$ – $.08$). As with AUC, parent support interacted with depressive symptoms to predict CRP ($b = -.20$, $SE = .07$). Again, parent support was split at the standardized mean ($z = 0$) and follow-up regressions were estimated to examine the simple-effect associations between depressive symptoms and CRP for those high and low in parent support. Fig. 4 shows that higher levels of depressive symptoms were associated with higher levels of CRP for individuals who reported low levels of parent support ($b = .27$, $SE = .10$). This association was not significant for individuals who reported high levels of parent support ($b = -.15$, $SE = .10$). CRP values in Fig. 4 are

Table 4
Stepwise hierarchical regression models predicting serum-equivalent C-reactive protein from depressive symptoms, parent support and friend support.

	Parent Support		Friend Support	
	Step 1 <i>b</i> (<i>SE</i>)	Step 2 <i>b</i> (<i>SE</i>)	Step 1 <i>b</i> (<i>SE</i>)	Step 2 <i>b</i> (<i>SE</i>)
Intercept	-.67 (.14)**	-.73 (.14)**	-.67 (.14)**	-.67 (.14)**
Age	.27 (.07)**	.28 (.07)**	.27 (.07)**	.27 (.07)**
Gender	.06 (.08)	.07 (.07)	.06 (.08)	.06 (.08)
Latino	-.08 (.19)	-.06 (.19)	-.07 (.19)	-.08 (.19)
Asian	-.27 (.21)	-.25 (.21)	-.28 (.21)	-.28 (.21)
Other	.09 (.33)	-.05 (.32)	.10 (.33)	.10 (.33)
Parent Education	-.15 (.08)	-.15 (.08)	-.15 (.08)	-.15 (.08)
BMI	.60 (.08)**	.62 (.08)**	.60 (.08)**	.60 (.08)**
Depressive Symptoms	.03 (.08)	.01 (.08)	.03 (.07)	.03 (.07)
Support	.03 (.08)	.06 (.08)	.02 (.07)	.02 (.07)
Depressive Symptoms × Support		-.20 (.07)*		-.03 (.06)

Note. Converted CRP serum values were log-transformed before analyses. Gender was effect-coded such that males were coded -1 and females coded 1. European Americans were coded as the reference group for ethnicity. All other continuous predictors were mean-centered as z-scores.

* $p < .05$.

** $p < .01$.

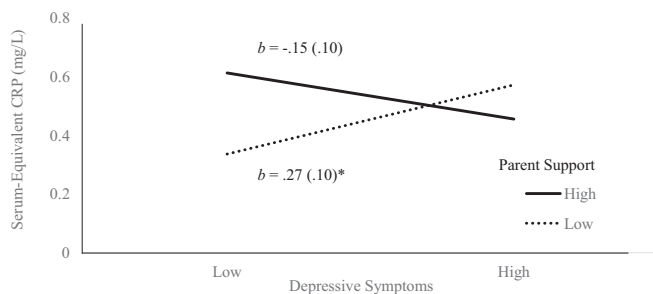


Fig. 4. Association between depressive symptoms and serum-equivalent CRP as a function of high and low parental support. Predicted values represented in the figure are based upon the final models in Table 4 and include all covariates.

non-logged for ease of interpretation. Additional analyses more precisely identifying regions of significance (Preacher et al., 2006) also indicated that slopes were non-significant between centered parental support values of $z = -.83$ to 1.29. Approximately 77.85% of participants had standardized parental support scores above and 22.15% had values below $-.83$. Fig. 3b shows regions of significant and non-significant simple slopes of depressive symptoms to CRP at conditional values of parent support. Friend support was not significantly related to CRP and did not moderate the association of depression with CRP ($b = -.03$, $SE = .06$). Follow-up three-way interactions by ethnicity and gender were not significant.

Discussion

The current study examined how social support from parents and friends may differentially buffer the link between depressive symptoms and biological markers of physical health during adolescence. Results indicated that parent support, but not friend support, moderated the links of depressive symptoms with HPA measures and CRP. Specifically, for adolescents who received low parent support, increasingly high levels of depressive symptoms were associated with increasingly higher cortisol output and inflammation. Additional analyses of diurnal cortisol indicate that this buffering was apparent for dynamic indices of daily output, particularly the CAR, but not for levels at singular time points (cortisol levels at wake and at bedtime). These findings are consistent with prior research that suggests that steeper morning rises are

associated with subsequent episodes of major depression among adolescents (Adam et al., 2010). The results here suggest that these patterns do not emerge for adolescents who received high parent support. Additionally, support from friends did not moderate these links.

The present study suggests that social support may be a particularly important coping mechanism to examine during adolescence in addition to other forms of coping (Low et al., 2013). Stress and depression during sensitive developmental periods may epigenetically increase glucocorticoid and pro-inflammatory gene expression (Miller et al., 2009; Nusslock and Miller, 2015). Experiences that suggest social disconnection can be perceived as a survival threat and strengthen this biological imprinting (Eisenberger and Cole, 2012). Positive experiences that disconfirm this threat of social exclusion and instead convey a sense of safety may disrupt these processes. The results here underscore the continued, and perhaps accumulated, importance of positive experiences with parents during adolescence (Fuligni and Eccles, 1993; Galambos et al., 2003; Helsen et al., 2000). These findings are in line with prior work showing that parents and peers may function independently of one another (Furman and Buhrmester, 1985; Helsen et al., 2000) and that positive relationships with parents may be particularly effective in promoting mental well-being during this developmental period (Lewinsohn et al., 1994; Stice et al., 2004; Windle, 1992).

Parent support did not moderate the association between depressive symptoms and cortisol levels at single time points (i.e., awakening, bedtime), but did significantly moderate the relationship between depressive symptoms and cortisol changes across the day (i.e., CAR, DCS). Inspection of the slopes for adolescents high and low in parent support suggested that the differential association was most evident for the CAR, where higher depressive symptoms were associated with a steeper CAR for those who reported low levels of parent support. That is, for those with low levels of parent support, group differences in cortisol levels, which were not apparent at time of awakening, began to emerge at 30 min after awakening. These high values in the morning slope may have affected the decline slope across the day. These differences in the morning CAR may also have contributed to the AUC measure and results. The link between depressive symptoms and the CAR for those low in parental support is consistent with work suggesting that the CAR may be a better indicator of future depression than other diurnal cortisol measure like morning and bedtime levels, total output across a day, and DCS (Adam et al., 2010).

Unexpectedly, higher friend support was associated with higher cortisol AUC. Also, the form of the parental support interaction in Fig. 2 suggested that adolescents low in depressive symptoms and high in parental support had higher AUC. These findings are intriguing considering that social support is believed to be related to positive health outcomes. This may be reflective of greater needs for support due to other individual differences and earlier experiences not measured in our study. For example, received support, as measured here, can be more context-dependent compared to perceived support, support that one feels is available but has not or does not need to be enacted (Uchino, 2009). That is, high levels of received support may be associated with higher levels of perceived stress and the need to ask for support, reflecting individuals who are actively adapting to their immediate environment. The finding for friend support may also highlight the greater potential for interpersonal conflict in interactions with peers (e.g., Rook, 1990). Whereas parents are perceived as more reliable sources of support, friendships are more likely to change over time and include elements of both acceptance and rejection (e.g., Stice et al., 2004). Moreover, although parent and friend support are positively correlated, they may act as separate and compensatory resources. That is, adverse childhood experiences and contentious parent-child relationships at home may lead to higher HPA activity and motivate adolescent reliance on friend support (Heim et al., 2000; Tarullo and Gunnar, 2006). Additionally, although the current study did not measure childhood maltreatment, childhood trauma might be a risk factor for depression during adolescence (Brown et al., 1999; Tarullo and Gunnar, 2006). The cross-sectional nature of this study precludes explanations and conclusions about directionality. Longitudinal analyses in the future would help disentangle the relationships found here.

Parent support also moderated the relationship between depression and CRP. This is consistent with prior work that suggests that sources of support vary in their moderation of distress to inflammation (Nakata et al., 2014) and that familial sources of support may be particularly important (Uchino et al., 1996). As with patterns of AUC, the interaction in Fig. 4 suggested that those high in parental support and low in depressive symptoms had higher CRP. It is important to note that CRP values for both high and low parental support groups were in the low risk category. Additionally, although similar patterns emerged in the relationship between depressive symptoms to HPA indicators and inflammation, CRP was notably not correlated with any of the HPA outcomes. This may be a feature of our healthy sample of young individuals. However, the association between higher depressive symptoms and higher CRP for those with low parent support may indicate the origins of an association that gets solidified in adulthood. In this way, the current study may contribute to our knowledge about the factors that disrupt or strengthen the coupling of depression and biological mechanisms linked to the development of physical health conditions.

It is believed that childhood stressors may be linked with inflammation in adulthood by promoting the formation of what Nusslock and Miller (2015) call a neuroimmune “pipeline” or “network,” in which pro-inflammatory signaling pathways between the brain and body are strengthened. Chen et al. (2011), for example, found that adults who experienced low SES early in their lives (an early stressor) who also experienced high maternal warmth had reduced pro-inflammatory profiles compared to those who experienced low maternal warmth. With regard to depressive symptoms, Miller and Cole (2012) found the clustering of depression and inflammation for individuals who had experienced childhood adversity but not in those who had not. Danese et al. (2011) similarly found higher CRP in children who reported depression and experienced maltreatment compared to those who reported depression alone or maltreatment alone. The current study aligns

with this prior research in finding that the association between depressive symptoms to hormonal dysregulation and inflammation is more evident in adolescents who reported low parent support compared to those who reported high parent support.

It is possible that the construct of self-reported parent support examined here may be biased by depressive symptoms themselves (e.g., depressed individuals may perceive lower levels of support compared to non-depressed individuals) or tapping into other protective factors, such as family cohesion or parenting style, that have been associated with mental health outcomes (Farrell and Barnes, 1993; Galambos et al., 2003; Uchino, 2009). Current mental health and early family experiences may contribute to creating “positive psychosocial profiles” that predispose individuals to perceive more support from others, more effectively use coping strategies, and otherwise alter the mechanisms through which social support affects health (Uchino, 2009). Therefore, future studies would benefit from examining other family and peer factors that may moderate adolescent health risk.

Other limitations with the scales used in the current study should be noted. The depressive symptoms measure in this study was not a diagnostic measure of clinical depression and the results reflect associations among a relatively healthy population of adolescents. Also, we focused on a functional measure of social support (e.g., instrumental, emotional support) rather than structural (e.g., number of friends, frequency of contact) and this may contribute to the heterogeneity of results across the literature (Uchino et al., 2012, 1996). Given the strong link between social integration to mortality (Berkman and Syme, 1979; House et al., 1988; Seeman, 1996), other behavioral mechanisms that link social relationships to health bear examination.

Despite the limitations, this study contributes to the literature in showing that the importance of parent support for diverse groups of adolescents may extend to physical well-being as well as mental well-being. It also contributes to our knowledge about the factors that may influence the coupling of depression and biological mechanisms under chronic stress. Together, these results support prior research on the important role of parental factors on adolescent health despite social network changes and growing autonomy concerns during this period.

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