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Borderline personality pathology, health behavior, and inflammation: Potential behavioral and biological mechanisms underlying childhood physical abuse and age-related disease

Christina R. Di Iorio¹, Sara A. Norton¹, Michael Boudreaux¹, Katharine K. Chang¹, Lindsay J. Michalski¹, Patrick J. Cruitt¹, Jonathan M.A. Winstone¹, Thomas F. Oltmanns¹, Ryan Bogdan¹

¹Department of Psychological and Brain Sciences, Washington University in St. Louis, St. Louis, MO, USA

Corresponding Author: Ryan Bogdan
WUSTL, Psych & Brain Bldg, CB 1125
One Brookings Drive
St. Louis, MO 63130
Phone: 617-407-5645; emails: rbogdan@wustl.edu

ABSTRACT

Background: The frequent comorbidity of psychiatric and physical health conditions may be partially attributable to early life stress-related changes in inflammatory signaling and behavior (e.g., borderline personality pathology, health behaviors) that reciprocally maintain and enhance their effects on overall health.

Methods: Using data from older adults ($N=1,630$) who participated in the ongoing longitudinal St Louis Personality and Aging Network (SPAN) study, we examined associations between childhood physical abuse, borderline personality pathology, inflammation markers (i.e., interleukin-6 [IL-6], C-reactive protein [CRP]), health behaviors, and physical health. Morning fasting serum IL-6 and CRP were assayed from a subset of participants ($n=791$). Borderline pathology factor scores were computed using interviews as well as self- and informant-reports across the course of the study. Physical health, health behaviors, and additional covariates (e.g., medication use) were also assessed.

Results: IL-6 was associated with higher BPD symptomatology, greater exposure to childhood physical abuse, worse physical health, and lower preventative health behaviors (all p values $< 10^{-11}$). Similar findings for CRP emerged, though the association with childhood physical abuse was not robust to covariate inclusion. An integrated model suggests an indirect pathway between exposure to childhood physical abuse, greater BPD symptomatology, reduced preventative health behaviors, elevated IL-6, and worse health outcomes ($-0.07, p < .001$).

Conclusions: These findings suggest that physical abuse during childhood may be predictive of later poor physical health through behavioral (i.e., borderline pathology, reduced preventative health behaviors), and biological (i.e., inflammatory) pathways.

INTRODUCTION

The effects of adversity during childhood have a lingering impact on psychological and physical health that extends into adulthood and later life (Afifi et al., 2011; Elwenspoek et al., 2017; G. E. Miller et al., 2011; Newnham & Janca, 2014). For instance, estimates suggest that early life stress (ELS) is associated with a substantial portion of psychiatric disorders (45% of childhood onset disorders and 26-32% of adolescent/adult-onset disorders; (Green et al., 2010) and greater odds of physical illness (e.g., cardiovascular disease: OR: 1.3-1.7; (Dong et al., 2004). However, the potential pathways that may contribute to the comorbidity of mental and physical health conditions and their frequent association with ELS remain poorly understood. Influential theoretical work pioneered by Miller, Chen, and Parker suggests that psychiatric and physical health comorbidities may be partly attributable to ELS-related changes in inflammation (e.g., a proinflammatory phenotype) and behavior (e.g., impulsivity, reduced preventative health behaviors) that reciprocally maintain and enhance their collective effects on general health (G. E. Miller et al., 2011; Nusslock & Miller, 2016).

Borderline personality pathology (BPP), which consists of pervasive affective instability, environmental reactivity, inconsistency in self-image, interpersonal dysfunction, and high levels of impulsivity, may contribute to ELS-related physical ailments in later life. *First*, borderline personality has been robustly linked to childhood maltreatment and abuse (e.g., ORs of 2.04-2.47; (Afifi et al., 2011). *Second*, BPP is commonly comorbid with internalizing and externalizing psychopathology, as well as physical health conditions (e.g., cardiovascular disease, diabetes, obesity, and arthritis; (Dixon-Gordon et al., 2015; El-Gabalawy et al., 2010; Powers & Oltmanns, 2013a), somatic syndromes (e.g., fibromyalgia and chronic fatigue; (Frankenburg & Zanarini, 2004), and subjective health complaints (Powers & Oltmanns, 2013b). Relatedly, as a general

factor of personality pathology (Sharp et al., 2015) it may represent a critical clinical construct with widespread implications for understanding comorbidity, similar to unifactoral models of non-personality psychopathology (Lahey et al., 2012). *Third*, evidence suggests that preventative health behaviors may be an intervening behavioral mechanism through which psychopathology and inflammation are related (G. E. Miller et al., 2011). BPP is associated with reduced preventative health behavior (e.g., reduced exercise; (Keuroghlian et al., 2013), which has independently been linked to elevated inflammation and worse physical health (Dankel et al., 2017; Hamer et al., 2012). *Fourth*, the limited data examining inflammation in the context of borderline personality disorder suggests that it may be associated with elevated systemic inflammation (Kahl et al., 2005, 2006, 2009; patient Ns-12-22). Guided by theoretical models (G. E. Miller et al., 2011), these data collectively raise the intriguing possibility that childhood abuse may precipitate the development of borderline personality pathology which, in turn, may contribute to reduced preventative healthcare, increased inflammation, and worse physical health later in life.

Using data ($N=1,630$) from adults ages 60-72 who have participated in the ongoing longitudinal St Louis Personality and Aging Network (SPAN) study (Oltmanns et al., 2014), we examined associations between childhood physical abuse, borderline personality pathology, inflammation markers (i.e., IL-6 and CRP), preventative health behaviors, and a global index of physical health. We hypothesized that childhood abuse would be indirectly linked to worse physical health through borderline personality pathology, and would be associated with fewer preventative health behaviors and elevated inflammation. Based on meta-analytic evidence that physical abuse in childhood is linked to elevations in IL-6, but not CRP, we expected that the link between childhood physical abuse and inflammation would be stronger for IL-6, and potentially absent for CRP (Baumeister et al., 2016).

METHODS

Participants and Procedure

The SPAN study is an ongoing longitudinal protocol assessing a wide range of personality, health, social, and biological characteristics in a representative community sample of 1,630 older adults (ages 55-64 at baseline) residing in the St. Louis, Missouri area (Iacovino et al., 2016). Recruitment details are provided in **Supplemental Information**. Each participant completed a 3-hour in-person assessment at baseline ($N=1,630$; baseline). Data for the current analyses also come from two subsequent in-person follow-up (FU) sessions occurring approximately 2.5 and 6 years after baseline (FU1, FU2). A fasting blood sample was collected from participants shortly after FU2 ($n=791$). Participants were also asked to complete a short sequence of mailed or online FU questionnaires in between in-lab sessions, although data from these waves of data collection were not used in the current analyses. All participants consented to the SPAN protocol, which was approved by the Washington University in St. Louis Institutional Review Board. They received \$20 remuneration for the blood draw, as well as \$60 for each in-person session and \$10 for each mailed or online follow-up questionnaire completed. Ninety percent of participants ($n=1,467$) also identified an individual that knew them well and could describe their personality to serve as their informant. Informants completed online or mailed questionnaires about each participant's personality (see **Supplemental Information** for additional informant details). For a timeline of assessments used in the current analyses, see **Figure 1**.

Measures

Borderline Personality Factor Scores

Borderline pathology was assessed using a dimensional approach from multiple perspectives (i.e., clinician, self, and informant ratings). We adopted a dimensional as opposed to a categorical (i.e., presence of diagnosis) approach to model borderline pathology across our non-selected community sample. In light of evidence that many people exhibit at least some personality pathology symptoms (Oltmanns et al., 2014), and that subthreshold borderline personality disorder symptoms are associated with psychosocial impairment (Ellison et al., 2016; Zimmerman et al., 2013), scores were treated continuously to retain variation at subthreshold diagnostic levels. Borderline pathology was assessed using multiple sources and methods to improve our coverage of subthreshold presentations of borderline pathology. We included informant reports because they add unique information about an individual's personality that the participant may be unable or unwilling to report (Oltmanns & Turkheimer, 2009) and are predictive of physical health outcomes over and above self-report (Jackson et al., 2015; Kneip et al., 1993). Clinician ratings of borderline pathology were acquired using the Structured Interview for DSM-IV Personality (SIDP-IV; (Pfohl et al., 1997); self- and informant reports were collected using the Revised NEO Personality Inventory (NEO PI-R; (Costa & McCrae, 1992) and the Multisource Assessment of Personality Pathology (MAPP; (Oltmanns & Turkheimer, 2006) as described below.

Clinical Interview: The SIDP-IV is a semi-structured interview in which trained interviewers rate 80 items corresponding to criteria of the 10 PDs on a scale of 0 (no pathology present) to 3 (pathology strongly present). SIDP scores were treated continuously by summing responses across the 9 BPD criteria. All interviews were conducted by graduate students in clinical psychology and trained undergraduate research assistants and interrater reliability ratings from a

selected subsample of 265 video-recorded interviews was excellent (intraclass correlation coefficient: 0.77; (Oltmanns et al., 2014).

Self and Informant Report: The NEO PI-R (Form S for self; Form R for informant) consists of 240-items assessing the five domains of neuroticism, extraversion, openness, agreeableness, and conscientiousness, as well as six lower-order facets within each domain. NEO PI-R borderline pathology scores were generated independently for self and informant report by summing anxiety, angry hostility, depression, impulsiveness, vulnerability, openness to feelings, openness to actions, compliance (reverse scored), and deliberation (reverse scored) facet scale scores (J. D. Miller et al., 2004). The MAPP is an 80-item measure of personality pathology based on lay translations of DSM-IV PD diagnostic criteria. Self- and informant MAPP BPD scores were calculated by summing responses across the 9 BPD items

We performed an exploratory structural equation modeling (ESEM) analysis on BPD scores derived from interview (SIDP-IV) and self- and informant-report (NEO PI-R and MAPP) data collected at the Baseline, FU1, and FU2 assessments using maximum likelihood estimation in Mplus 7.3 (Muthén & Muthén, 1998). We hypothesized a one-factor model to account for the correlations among the 15 BPD measures (i.e., self and informant report and clinician ratings across assessment times). However, because the unique components of the same measure administered on different occasions are likely to be correlated, we included them in the a priori model. An evaluation of model fit with these correlated residuals resulted in an improvement in fit as compared to a baseline model without them (RMSEA = .115, CFI = .867, TLI = .813 vs. RMSEA = .184, CFI = .588, TLI = .520) but still does not provide an acceptable fit to the data. Modification indices suggested that the error terms correlated across method (e.g., participant MAPP with NEO, informant MAPP with NEO), and were therefore estimated in a subsequent

model. This resulted in very good to excellent model fit (RMSEA = .056, CFI = .976, TLI = .955) according to conventional criteria (Hu & Bentler, 1999). Factor loadings in this model ranged from .45 to .70. Factor scores were estimated and saved for use in all subsequent analyses.

Childhood Physical Abuse

The 28-item Childhood Trauma Questionnaire (CTQ; (Bernstein et al., 2003; Scher et al., 2001) was used to retrospectively assess emotional, physical, and sexual abuse as well as emotional and physical neglect before the age of 17. Our decision to focus specifically on childhood physical abuse was two-fold. First, meta-analytic findings suggest that trauma type differentially impacts inflammatory dysregulation (Baumeister et al., 2016), such that childhood physical abuse has been consistently linked to increased IL-6, but not CRP. Second, autobiographical memory research finds that physically painful life events are more deeply encoded and therefore more easily recollected than less physically threatening experiences (Rubin & Kozin, 1984). Additionally, older adults have a greater propensity for recalling more emotionally positive than negative events (Kennedy et al., 2004; Schlagman et al., 2006). Accordingly, identifying neglect may be more difficult within our older cohort, while autobiographic memories associated with physical/sexual trauma are likely to be preserved due to their increased salience. This is supported by evidence that discrepancies arising from retrospective reports of early life stress occur most in the detection of less severe (i.e., single occurrence or less physically evident) cases of maltreatment (Shaffer et al., 2008).

Global Physical Health and Health Behaviors

Global physical health was assessed at Baseline and FU2 using the physical health composite (i.e., physical functioning, role limitations due to physical problems, pain, and general health

perceptions) of the 36-item Health Status Inventory (Hays & Morales, 2001). Preventative health behaviors were assessed at FU2 using the 40-item Health Behavior Checklist (Vickers et al., 1990). Factor analytic evidence supports a two-factor model for the Health Behavior Checklist, composed of preventative (i.e., avoiding or minimizing effects of accidents and maintaining or enhancing wellness) and risk-taking behavior (i.e., risk taking behaviors and substance use). Due to the strong association between preventative health behaviors and inflammation (Anderson et al., 2012; Richard et al., 2013; Yates et al., 2008), we used this variable in our study.

IL-6 and CRP

Morning fasting blood samples were collected between 7:30-10:00 am via peripheral (primarily antecubital) venipuncture in an independent session closely following the FU2 assessment (typically within two weeks) from consenting participants ($n=791$). Samples were not obtained from any participants reporting acute illness or injury. Serum was collected in silicon-coated tubes with no additives and left at room temperature for 40 – 60 minutes to allow for clot formation. Samples were centrifuged (1300 g) for 20 minutes and then immediately transferred into 2 mL tubes and stored at -80° C until the day of the assay.

IL-6 and CRP were assayed in duplicate using commercially available enzyme-linked immunosorbent assays (IL-6: Quantikine HS Human IL-6 ELISA, R&D Systems, Minneapolis, MN, USA; CRP: EIA-3954 High Sensitivity C-Reactive Protein ELISA DRG International Inc., USA). Intra- (IL-6: 5%, CRP: 4%) and inter- (IL-6: 14%, CRP: 13%) assay coefficients of variation were acceptable. Samples producing unreliable measures (i.e., intra-assay CVs >20%) of IL-6 ($N=38$; 4.8%) or CRP ($N=22$; 2.8%), even after being re-assayed in duplicate were excluded, leaving 753 and 769 measured data points for IL-6 and CRP, respectively.

204 ***Other Relevant Covariates***

205 ***Age*** at the blood draw session was calculated using the participants' date of birth and the date of
 206 their blood draw appointment. Body Mass Index (***BMI***) and Mean Arterial Pressure (***MAP***) were
 207 directly measured (Life Source model UA-789) at the blood draw appointment. ***Medication*** use
 208 was assessed using lists of all current prescription drugs, over the counter medications, and
 209 supplements provided by participants at the FU2 interview and phlebotomy session. Medications
 210 were logged within the following medication classes: statin (n=307), beta blocker (n=172),
 211 calcium blocker (n=161), ACE inhibitor (n=303), benzodiazepines (n=50), hormonal medications
 212 (n=72), aspirin (n=296), prescription pain killer (n=98), NSAID (n=155), steroid medication
 213 (n=102), anti-depressant medication (i.e., a TCA, SSRI, or SNRI; n = 175). Average hours of sleep
 214 per night and caffeine use (e.g., number of caffeinated beverages consumed in the average day)
 215 were assessed at the phlebotomy session. ***Baseline physical health*** was assessed using the health
 216 status inventory, the same measures used at our FU2 outcome variable. ***Depressive symptoms*** were
 217 measured at the FU2 session using the Beck Depression Inventory-II (Beck et al., 1996). History
 218 of ever being a regular smoker (dichotomized as 0 vs 1) was assessed at baseline.

219 ***Statistical Analyses***

220 To maintain data variability but minimize the influence of extreme outliers, all outlier values on
 221 predictor variables of interest were winsorized to ± 3 SDs before conducting analyses. Further,
 222 consistent with prior literature, inflammation markers (i.e., IL-6, CRP) were log transformed prior
 223 to analyses. All predicted associations were tested using bivariate correlations with listwise
 224 deletion. Benjamini-Hochberg false-discovery rate (fdr) was used to adjust for multiple
 225 comparisons. All analyses other than the simple bivariate correlations and demographic
 226 comparisons were conducted using maximum likelihood (ML) estimation in *Mplus* to retain

missing data points. Any associations involving inflammation markers with evidence of significant bivariate correlation were further tested using a series of linear regressions with the following 20 covariates: age at blood draw, sex, self-reported ethnicity (i.e., white/not-white, Black/not-Black; Hispanic/not-Hispanic), BMI, MAP, sleep, caffeine, and medication class usage (see list in covariate section). Regressions not involving inflammation markers included the following 5 covariates: sex, white/not white, black/not black, Hispanic/not Hispanic, age. Our hypothesized mediational model included all 20 covariates included in our inflammation analyses on all paths (see also **Figure 2**). This analysis was repeated in 3 additional forms: (1) with the addition of baseline physical health and lifetime regular smoking status as covariates, (2) with the analysis just mentioned but using listwise deletion for missing data, and (3) with no covariates. As reported in the **Supplemental Information**, these different analytic approaches yielded a consistent pattern of results.

RESULTS

Participants Characteristics and Associations with Variables of Interest

Tables 1-3 detail participant characteristics on demographic and study-relevant assessments as well as their associations with our variables of interest (i.e., childhood physical abuse, borderline factor scores, IL-6, CRP, health behaviors, and global physical health). Briefly, self-reported ethnicity was significantly associated with all variables of interest except preventative health behaviors (**Table 1**). Relative to all others and European-Americans, African-Americans had higher inflammation and reported greater childhood abuse as well as more physical health problems, but had lower BPD factor scores. Compared to men, women had higher levels of CRP and engaged in more preventative health behaviors (**Table 2**). **Table 3** reports associations between covariates and study variables of interest. Briefly, age was negatively correlated with BPD and positively correlated with physical health. Perhaps unsurprisingly, given the existing literature (Ferrante, 2007; Kopelman, 2000; Powers & Oltmanns, 2013a), BMI was correlated with increased inflammation, increased BPD, worse physical health, and fewer preventative health behaviors. Similar patterns were observed with smoking (i.e. smoking was associated with worse physical health and fewer preventative health behaviors), though smoking was also positively correlated with childhood physical abuse. Sleep was associated with increased inflammation, greater reports of childhood abuse, greater borderline factor scores, better physical health, and more preventative health behaviors. Mean arterial blood pressure was associated with increased levels of CRP and worse physical health. Finally, medication usage (for respective associations, please see **Table 3**) was associated with inflammation, childhood abuse, BPD and physical health, but not preventative health behaviors.

Primary Analyses: Childhood Physical Abuse, Borderline Personality Pathology, Health Behavior, Inflammation, and Physical Health

Bivariate correlations between childhood physical abuse, borderline personality pathology preventative health behaviors, IL-6, CRP, and physical health are presented in **Table 4** with correction for multiple testing. Below we describe *fdr*-corrected correlations of hypothesized and other notable associations as well as these results when considering our covariates, and finally, our integrated mediational model.

IL-6 and ***CRP*** were both associated with increased childhood physical abuse and borderline personality pathology and decreased preventative health behaviors and physical health. ***Childhood physical abuse*** was predictive of elevated borderline personality pathology and worse physical health, although it was unrelated to preventative health behaviors. ***Borderline personality pathology*** was associated with reduced preventative health behaviors and worse physical health. ***Preventative health behaviors*** were negatively correlated with physical health. All of these associations were robust to the inclusion of our covariates, with the exception of the link between childhood physical abuse and CRP, which was reduced to a trend (see **Supplemental Table 1**).

As a result of meta-analytic evidence that CRP is not associated with childhood physical abuse (Baumeister, et al., 2016) as well as the lack of an association between childhood physical abuse and CRP after accounting for covariates in our sample, we did not include CRP in our mediational models. Suggestive of unique associations between borderline pathology and both IL-6 and CRP, these associations were robust to the additional inclusion of either childhood abuse (IL-6: $\beta = 0.11$, $p = 0.004$; CRP: $\beta = 0.11$, $p = 0.005$) or depression (IL-6: $\beta = 0.07$, $p = 0.02$; CRP: $\beta = 0.06$, $p = 0.05$, which was also uniquely associated with inflammation; **Supplemental Figure 2**; Bondy et al., 2021) in the model. However, consistent with the mediational model presented below,

the association between childhood physical abuse and IL-6 was not robust to the inclusion of
borderline pathology ($\beta=0.009$, $p=0.83$).

Our hypothesized model provides support for a serial indirect association wherein
childhood physical abuse is indirectly linked to worse physical health in later-life through
increased borderline pathology, reduced preventative health behavior, and increased inflammation
(**Figure 2; Supplemental Table 2**). This indirect association remained significant when baseline
physical health and lifetime regular smoking status were added to the model, when this analysis
was conducted using listwise deletion, or when no covariates were included (**Supplemental
Tables 3-4**).

DISCUSSION

The high comorbidity between mental and physical health conditions (Barnett et al., 2012; Quirk et al., 2016), and their unequivocal associations with early life stress (ELS; (Afifi et al., 2011; Elwenspoek et al., 2017; G. E. Miller et al., 2011; Newnham & Janca, 2014), suggest that common underlying pathways shaped by ELS may underlie their expression. Our study examined whether borderline personality pathology, health behaviors, and inflammation indirectly link childhood physical abuse to physical health in a large sample ($N=1,630$) of aging adults. Three findings within our study are particularly noteworthy. First, we find evidence that borderline pathology is associated with heightened inflammation (i.e., IL-6 and CRP) and that these associations are present even when considering childhood physical abuse or depression. Second, aligning with meta-analytic evidence (Baumeister et al., 2016), IL-6, but not CRP (when considering potential confounding covariates), was associated with childhood physical abuse. The association between CRP and childhood physical abuse was trending in our sample after accounting for potential confounding covariates; as such, this correlation may indeed reflect a meaningful association that could be uncovered, even in the context of covariates, within prospective studies before medication use and other related factors develop (e.g., obesity). Third, and most importantly, we find evidence for an indirect pathway wherein childhood abuse is indirectly linked to worse physical health in later-life through increased borderline personality pathology, reduced preventative health behavior, and increased inflammation (**Figure 2**). Broadly, these results support theoretical work advanced by Miller, Chen, and Parker (2011) that adversity encountered in childhood leads to biological (e.g., elevated inflammation) and behavioral (e.g., emotion dysregulation, impulsivity) programming that initiates, maintains, and exacerbates chronic inflammation to increase risk for later age-related disease. In particular, our data provide evidence that it is plausible that childhood

physical abuse may contribute to worse physical health in older age through behavioral (i.e., borderline personality pathology, health behaviors) and biological (i.e., inflammation) factors.

Borderline pathology was related to worse physical health as has been previously reported (Dixon-Gordon et al., 2015; El-Gabalawy et al., 2010; Frankenburg & Zanarini, 2004; Powers & Oltmanns, 2013a), as well as increased inflammation (Kahl et al., 2005, 2006, 2009). Notably, we are only aware of three prior studies of borderline personality pathology and inflammation, all of which found evidence of increased inflammation – and in particular IL-6 levels – among patients with comorbid borderline personality disorder and major depressive disorder (patient Ns-12-22; Kahl et al., 2005, 2006, 2009). Our study critically extends this work by showing that borderline personality pathology present in the general population is associated with elevated IL-6 and CRP, and further, that these relationships are present even after accounting for depressive symptoms (**Supplemental Figure S3**), and childhood physical abuse (**Supplemental Tables 1-2**). Thus, our data suggest that borderline personality pathology, even in subclinical forms, has unique associations with inflammation beyond its common comorbidity with childhood adversity and depressive symptoms, and that such increased inflammation may arise from borderline personality pathology associated reductions in preventative health behaviors (El-Gabalawy et al., 2010; Frankenburg & Zanarini, 2004), to increase risk for age-related physical health conditions. That borderline personality pathology is associated with inflammation, an objective index of physical health is notable and suggests that elevated complaints of physical health among individuals with borderline personality pathology may not be attributable to increased healthcare engagement.

Collectively, our data align with speculative theory that ELS-related behavioral proclivities may serve to initiate, maintain, and enhance risk for age-related physical health problems through inflammatory effects. A critical issue unaddressed by our data is whether inflammation linked to

physical abuse during childhood may elicit borderline personality pathology, the expression of which may further exacerbate greater systemic inflammation. While there is evidence to support such bidirectional associations between inflammation and psychopathology as well as related behavior (e.g., impulsivity; (Afifi et al., 2011); such data do not exist for borderline personality pathology specifically. We are unable to test such a model in our data because it would require measures across the entire lifespan (e.g., inflammation markers assessed during childhood prior to the development of borderline personality characteristics), that are unavailable in our sample.

It is important to consider the limitations of this study in its interpretation. First, our mediational model implies a direction of effect. While these models were built based upon prior evidence supporting their directionality (G. E. Miller et al., 2011), as well as their temporal assessment in our study, the lack of multiple measures for each phenotype (e.g., inflammation) across the lifespan did not permit us to evaluate whether change in each variable temporally precedes change in another. However, given our life course perspective, variables would need to be assessed throughout life (e.g., inflammation measures among newborns and in childhood before abuse), and ideally, even prenatally and across generations. Within our model, we temporarily anchor childhood adversity (retrospective report collected at FU2) as preceding borderline pathology (assessed at baseline, FU1, and FU2 with clinician, self- and informant-report; stable across time in adulthood) and inflammation (collected at FU2) based on foundational literature showing that physical abuse is associated with borderline personality pathology and inflammation in adulthood (Baumeister et al., 2016; Newnham & Janca, 2014). Further, though preventative health, inflammation, and physical health were not temporally discernable based on timing of data collection (all information collected at FU2), we posited directionality guided by theoretical hypotheses (Afifi et al., 2011) and extant literature suggesting the effect of preventative health

behaviors on both inflammation and physical health (Anderson et al., 2012; Richard et al., 2013; Yates et al., 2008). Moreover, we were able to include our physical health composite as assessed during our baseline visit as a covariate, suggesting that our observed effects are not attributable to pre-existing health problems. Notably, baseline physical health also indirectly links childhood physical abuse to later physical health problems in parallel to our serial mediational pathway. This pathway may represent the presence of additional pathways to poor health, but may also reflect the same serial indirect pathway occurring at an earlier time (e.g., it is possible that BPP pathology, preventative health behaviors and inflammation occurring prior to the baseline health assessment provide an indirect link). In addition to constraining conclusions about temporality, estimates generated by our mediational model may be biased because components in our mediational model (e.g., retrospective report of ELS, inflammation, preventative health behaviors, and physical health) were collected at the same time point.

Second, consistent with literature showing that BPD “matures out” with age (Shea et al., 2009; Zanarini et al., 2012), only 0.4% of our sample met diagnostic (e.g., DSM-5) criteria for BPD, which is less than an epidemiological study identifying a prevalence rate of 2.7% (NESAR: Tomko et al., 2014). Despite evidence that certain maladaptive personality traits are less common in older adulthood, previous research using data from the SPAN study shows that these traits continue to contribute unique variance to the prediction of stressful life events, marital satisfaction and physical health in later life (Gleason et al., 2014). BPD, in particular, exhibits associations with negative health perceptions and increased healthcare utilization at six-month follow-up in this sample (Powers & Oltmanns, 2013b), and is related to arthritis and heart disease, with obesity partially mediating these associations (Powers & Oltmanns, 2013a). Additionally, focusing on an older adult sample was important for the purposes of our study as it afforded us the unique

388 opportunity to explore the physical health issues related to the aging immune system, which leads
389 to greater susceptibility to illness and increased frequency of new health problems onset (Ginaldi
390 et al., 2001; Gruver et al., 2007).

391 Third, our measure of childhood physical abuse was measured using retrospective self-
392 report, which may introduce error in report. However, given evidence of less error among
393 retrospective reports of salient or severe events (Schlagman et al., 2006), such as physical abuse,
394 as well as the demonstrated convergent validity of our questionnaire with clinician-rated childhood
395 abuse interviews (Scher et al., 2001) these concerns may be minimal. Moreover, identified
396 reporting bias tends to lead to underreporting of maltreatment (Hardt & Rutter, 2004; Shaffer et
397 al., 2008); such error may induce noise into our model and reducing our power to detect
398 associations.

399 Finally, it is important to recognize that a representative community sample does not mean
400 a sample devoid of pathology. Forty-four percent of the current sample indicated that they
401 “received treatment for a mental disorder or advice from a mental health professional on problems
402 in life” at some point in their lifetime (Lawton & Olthmanns, 2013). At the same time, clinical
403 samples would likely exhibit greater psychiatric medication usage and comorbidity between BPD
404 and other psychiatric conditions, making it harder to control for the effects of these sample
405 characteristics. Additionally, our findings using a dimensional approach to personality pathology
406 highlight the fact that, even in individuals who exhibit subthreshold levels of BPD symptoms,
407 these effects on preventative health behaviors and physical health outcomes are significant.
408 Although we consider the representativeness of the current sample as a strength of the current
409 analyses, it will be important to replicate these results in a clinical sample with greater rates of
410 individuals who meet full criteria for BPD.

Limitations notwithstanding, our results support theory positing that childhood stress-related immune function plays an important role in the development of comorbid mental health and physical health disorders (G. E. Miller & Blackwell, 2006; Nusslock & Miller, 2016). The observed indirect association suggests that borderline personality pathology and related preventative health behavior as well as inflammation may represent behavioral and biological mechanisms linking childhood physical abuse to poor physical health in later life. As such, these represent potential therapeutic targets to reduce the impact of childhood adversity on later health.

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425

426 DISCLOSURES

427 No authors report financial relationships with commercial interests relevant to this research
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Figure 1. A timeline of study assessments included in analyses. Borderline personality pathology was defined by a factor score, which was calculated from the clinician-rated Structured Interview for DSM-IV Personality (SIDP-IV), and both the self and informant versions of the Revised NEO Personality Inventory (NEO-PI-R) and the Multisource Assessment of Personality Pathology (MAPP). Childhood physical abuse was assessed with the Childhood Trauma Questionnaire (CTQ). Global physical health was assessed with the physical health composite of the Health Status Inventory (HSI). Preventative health behaviors were assessed with the Health Behavior Checklist (HBC). Lastly, IL-6 and CRP were assayed from blood samples collected during a fasting blood draw shortly after FU2.

Figure 2: The relationship between childhood physical abuse and worse physical health in later life is accounted for by borderline personality pathology, preventative health behaviors, and IL-6. An integrated model suggests an indirect pathway between childhood abuse, greater BPD symptomology, reduced preventative health behaviors, elevated IL-6, and worse health outcomes. Covariates included, age, sex, 19 medication classes, caffeine consumption, and sleep. Pathways represent non-standardized coefficients and bootstrapped 95% confidence intervals. The association between childhood abuse and physical health was entirely accounted for by this indirect pathway (without BPD, preventative health behaviors, and IL-6, the association between childhood physical abuse and physical health was -4.401, $p = 0.05$).

639 **Table 1. Associations with Ethnicity**

	European American Total N=1061			African American Total N= 516			Hispanic Total N= 39					
	N	Mean (SD)	t/ χ^2	N	Mean (SD)	t/ χ^2	N	Mean (SD)	t/ χ^2	n	Mean (SD)	Timepoint
<i>Covariates of Interest</i>												
IL-6	542	0.23 (0.28)	-3.91***	195	0.32 (0.29)	3.40**	18	0.28 (0.23)	0.30	753	0.26 (0.29)	FU2
CRP	551	0.35 (0.51)	-5.02***	201	0.56 (0.51)	4.73***	18	0.51 (0.39)	0.82	769	0.41 (0.52)	FU2
Childhood Physical Abuse	744	1.06 (1.54)	-9.93***	284	0.88 (0.14)	9.47***	22	.82 (0.11)	0.32	1052	0.81 (0.13)	FU1
Borderline Pathology	1061	0.01 (1.02)	0.63	516	-0.06 (1.04)	-1.48	30	-0.14 (0.79)	-0.570	1630	-.00001 (1.04)	B, FU1, FU2
Preventative Health Behaviors	742	0.83 (0.90)	4.61***	286	-0.20 (0.91)	-4.30***	22	-0.22 (0.81)	-1.11	1053	-0.01 (0.92)	FU2
Physical Health	741	60.93 (8.91)	6.51***	274	56.29 (11.05)	-6.03***	20	62.75 (6.62)	2.10	1039	59.57 (9.81)	FU2 ^a
<i>Covariates of No Interest</i>												
Age	570	65.92 (2.87)	-0.01	204	66.02 (2.97)	0.59	18	65.17 (2.38)	-1.12	791	65.92 (2.89)	FU2
Gender (# women)	577	54.38% women	$\chi^2=0.29$	291	56.40% women	$\chi^2=0.72$	13	43.33% women	$\chi^2=1.69$	1617	54.9% woman	FU2
BMI	654	29.40 (6.56)	-4.27***	251	31.60 (7.17)	4.28***	18	32.45 (5.52)	1.85	924	.02 (6.91)	FU2
Beta Blockers	617	0.18 (0.39)	-2.01*	225	0.25 (0.44)	2.20**	18	0.11 (0.32)	-1.16	860	0.20 (0.40)	FU2
Calcium Channel Blockers	617	0.13 (0.34)	-5.97***	225	0.33 (0.47)	5.77***	18	0.11 (0.32)	-0.84	860	0.19 (0.39)	FU2
Statins	617	0.36 (0.48)	-0.04	225	0.38 (0.49)	0.76	18	0.22 (0.43)	-1.34	860	0.36 (0.48)	FU2
ACE/ARBs	617	0.32 (0.24)	-2.85**	225	0.44 (0.50)	3.28**	18	0.22 (0.43)	-1.29	860	0.35 (0.48)	FU2
Benzodiazepines	617	0.06 (0.24)	1.01	225	0.04 (0.21)	-1.10	18	0.06 (0.24)	-0.05	860	0.06 (0.23)	FU2
Hormone Medications OC/HT	617	0.10 (0.29)	2.25*	225	0.05 (0.23)	-2.17	18	0.00 (0.00)	-8.87***	860	0.08 (0.28)	FU2
Aspirin	617	0.34 (0.48)	-0.22	225	0.35 (0.48)	0.09	18	0.44 (0.51)	0.91	860	0.34 (0.48)	FU2

Rx Pain	617	0.10 (0.30)	-2.05*	225	0.15 (0.36)	1.88*	18	0.00 (0.00)	-10.53***	860	0.11 (0.32)	FU2
Non-Steroidal Anti-Inflammatory Drugs	617	0.19 (0.39)	1.18	225	0.16 (0.36)	-1.16	18	0.17 (0.38)	-0.153	860	0.18 (0.39)	FU2
Steroid Medications	617	0.11 (0.31)	-1.16	225	0.14 (0.35)	1.21	18	0.06 (0.24)	-0.84	860	0.12 (0.32)	FU2
Antidepressants	617	0.23 (0.42)	2.94**	225	0.14 (0.35)	-3.13**	18	0.17 (0.38)	-0.84	860	0.20 (0.40)	FU2
Mean Arterial Pressure	626	101.19 (13.75)	-4.25***	244	106.01 (15.59)	4.52***	18	107.37 (10.26)	-0.39	888	102.50 (14.38)	FU2
Baseline Physical Health	1040	60.99 (8.72)	9.68***	501	55.63 (11.12)	-9.20***	29	62.66 (6.38)	2.90**	1578	59.14 (9.97)	FU2
Sleep	490	7.10 (1.10)	9.27***	187	6.03 (1.47)	-8.79***	17	7.26 (0.97)	2.01	694	6.79 (1.30)	FU2
Caffeine	490	2.52 (1.69)	7.25***	187	1.54 (1.42)	-7.57***	17	2.24 (2.03)	-0.04	694	1.55 (0.50)	FU2
Smoking	1061	3.23 (5.41)	-0.45	516	3.24 (6.02)	-0.16	30	3.40 (5.19)	0.13	1630	3.24 (5.69)	B

*p<0.05, **p<0.01, ***p<0.001

Timepoint at which variable assessed is denoted as follows: B= Baseline; FU1= Follow-up 1; FU2= Follow-up 2. All analyses conducted using listwise deletion. ^a Physical health at baseline was also included as a covariate

644 **Table 2. Associations with Gender.**

	Women		Men		t/ χ^2
	N	Mean (SD)	N	Mean (SD)	
Covariates of Interest					
IL-6	410	0.25 (0.28)	343	0.27 (0.30)	-1.10
CRP	414	0.48 (0.53)	355	0.33 (0.49)	4.19***
Childhood Physical Abuse	572	6.85 (2.75)	480	6.86 (2.35)	0.90
Borderline Pathology	887	30.04 (1.05)	730	-0.04 (1.04)	-1.53
Preventative Health Behaviors	571	0.08 (0.86)	481	-0.12 (0.96)	3.36**
Physical Health	563	59.16 (9.99)	476	60.06 (9.58)	-1.48
Covariates of No Interest					
Age	426	65.97 (2.92)	365	65.87 (2.87)	0.50
European American	577	54.38% EA	484	45.62% EA	$\chi^2=0.29$
African American	291	56.40% AA	225	43.60% AA	$\chi^2=0.72$
Hispanic Ethnicity	13	43.33% His	17	56.67% His	$\chi^2=1.69$
BMI	499	30.91 (7.90)	425	28.98 (5.36)	4.38
Beta Blockers	467	0.21 (0.41)	393	0.19 (0.40)	0.44
Calcium Channel Blockers	467	0.21 (0.41)	393	0.17 (0.37)	1.52
Statins	467	0.32 (0.47)	393	0.40 (0.49)	-2.24*
ACE/ARBs	467	0.32 (0.47)	393	0.39 (0.49)	-2.08*
Benzodiazepines	467	0.07 (0.26)	393	0.40 (0.20)	1.75
Hormone Medications OC/HT	467	0.11 (0.32)	393	0.05 (0.22)	3.30**
Aspirin	467	0.30 (0.46)	393	0.40 (0.49)	-3.27**
Rx Pain	467	0.14 (0.35)	393	0.08 (0.28)	2.59*
Non-Steroidal Anti-Inflammatory Drugs	467	0.22 (0.41)	393	0.14 (0.35)	3.06**
Steroid Medications	467	0.15 (0.36)	393	0.08 (0.28)	2.95**
Antidepressants	467	0.27 (0.45)	393	0.12 (0.33)	5.86***
Mean Arterial Pressure	477	101.00 (14.64)	411	104.24 (13.88)	-3.37**
Baseline Physical Health	865	58.57 (10.2)	712	59.82 (9.61)	2.49*
Sleep	371	6.80 (1.31)	323	6.78 (1.29)	0.23
Caffeine	371	2.17 (1.65)	323	2.34 (1.70)	-1.36
Smoking	887	3.09 (5.48)	730	3.48 (5.97)	1.37

*p<0.05, **p<0.01, ***p<0.001. All analyses conducted using listwise deletion.

647 **Table 3. Sample Demographics and Associations with Model Variables**

Variable	N or Mean $\pm$ Std Dev	Correlations (r) with variables of interest:					
		IL-6	CRP	Physical Abuse	BPD	Physical Health	Prevent Health Behaviors
White/not White ^a	1061	-0.14***	-0.18***	-0.30***	0.02	0.22***	0.14***
Black/not Black ^a	516	0.12***	0.17***	0.29***	-0.04	-0.20***	-0.13***
Hispanic/not Hispanic ^a	30	0.01	0.03	0.01	-0.02	0.05	-0.03
Gender ^a	730 male	-0.04	0.15***	-0.03	-0.04	-0.05	0.10**
Age	65.92 $\pm$ 2.89	-0.01	0.02	-0.06	-0.09*	0.10**	0.08*
BMI	30.02 $\pm$ 6.91	0.32***	0.42***	0.05	0.09**	-0.33***	-0.21***
Beta Blockers	172	0.15***	0.08*	0.07	0.02	-0.20***	-0.01
Calcium Channel Blocker	161	0.14***	0.14***	0.08*	-0.02	-0.16***	-0.02
Statins	307	0.12***	0.02	0.04	0.05	-0.10**	-0.03
ACE/ARBs	303	0.17***	0.16***	0.05	0.04	-0.19***	-0.04
Benzodiazepines	50	0.04	0.01	0.003	0.22***	-0.16***	-0.03
Hormone medications OC/HT	72	-0.14***	-0.08*	0.07*	0.02	0.09**	0.11***
Aspirin	296	0.09*	0.04	-0.01	-0.04	-0.14***	-0.02
Rx Pain	98	0.24***	0.12***	0.05	0.08*	-0.34***	-0.02
Non-Steroidal Anti Inflammatory Drugs	155	0.01	0.02	-0.06	0.08**	-0.14***	0.03
Steroid Medications	102	0.08*	0.10**	-0.01	0.07	-0.13***	0.05
Antidepressants	175	0.11**	0.06	0.09*	0.31***	-0.27***	-0.10**
Mean Arterial Pressure	102.50 $\pm$ 14.38	0.06	0.09*	0.04	-0.003	-0.10**	-0.05
Baseline Physical Health	59.14 $\pm$ 9.97	-0.26***	-0.20***	-0.19***	-0.36***	0.71***	-0.27***
Sleep	6.79 $\pm$ 1.30	-0.14***	-0.10**	-0.21***	-0.12**	0.23***	0.18***
Caffeine	2.25 $\pm$ 1.68	-0.02	-0.13**	-0.06	0.07	0.03	-0.06
Smoking	3.24 $\pm$ 5.69	0.20***	0.11**	0.16***	0.38***	-0.49***	-0.29***

648 ***p $\leq$ 0.001; **p $\leq$ 0.01; *p $\leq$ 0.05. All analyses conducted using listwise deletion.649 ^aCoded as White=1, not White = 0. Self-reported gender was coded as 0=male, 1 = female

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Table 4. Associations Between Childhood Physical Abuse, Borderline Personality Pathology, Health Behaviors, Inflammation Markers, and Physical Health.

	IL-6	CRP	Childhood Physical/Sexual Abuse	Borderline Pathology	Preventative Health Behaviors
Childhood Physical Abuse	0.126** (n=738)	0.080* (n=754)	--	--	--
Borderline Pathology	0.165** (n=753)	0.092* (n=769)	0.256** (n=1052)	--	--
Preventative Health Behaviors	-0.302** (n=738)	-0.218** (n=754)	-0.081* (n=1050)	-0.256** (n=1052)	--
Physical Health	-0.0346**** (n=732)	-0.289*** (n=748)	-0.200** (n=1038)	-0.380**** (n=1039)	0.341*** (n=1038)

651 p-fdr is denoted as follows: * $p < 10^{-4}$; ** $10^{-4} < p < 10^{-11}$; *** $10^{-11} < p < 10^{-15}$; **** $p < 10^{-21}$