Brain, Behavior, and Immunity 53 (2016) 105–112

Contents lists available at ScienceDirect

Brain, Behavior, and Immunity

journal homepage: www.elsevier.com/locate/ybrbi

Associations of childhood adversity and adulthood trauma with C-reactive protein: A cross-sectional population-based study

Joy E. Lin [a,c,*], Thomas C. Neylan [b,c], Elissa Epel [b], Aoife O'Donovan [b,c,*]

[a] School of Medicine, University of California, San Francisco, 500 Parnassus Avenue, San Francisco, CA 94143, United States
[b] Department of Psychiatry, University of California, San Francisco, 500 Parnassus Avenue, San Francisco, CA 94143, United States
[c] San Francisco Veteran's Affairs Medical Center, 4150 Clement Street, San Francisco, CA 94121, United States

ARTICLE INFO

Article history:
Received 14 September 2015
Received in revised form 19 November 2015
Accepted 21 November 2015
Available online 23 November 2015

Keywords:
Childhood adversity
Adulthood trauma
C-reactive protein
Immune system
Inflammation

ABSTRACT

Mounting evidence highlights specific forms of psychological stress as risk factors for ill health. Particularly strong evidence indicates that childhood adversity and adulthood trauma exposure increase risk for physical and psychiatric disorders, and there is emerging evidence that inflammation may play a key role in these relationships. In a population-based sample from the Health and Retirement Study (n = 11,198, mean age 69 ± 10), we examine whether childhood adversity, adulthood trauma, and the interaction between them are associated with elevated levels of the systemic inflammatory marker high sensitivity C-reactive protein (hsCRP). All models were adjusted for age, gender, race, education, and year of data collection, as well as other possible confounds in follow-up sensitivity analyses. In our sample, 67% of individuals had experienced at least one traumatic event during adulthood, and those with childhood adversity were almost three times as likely to have experienced trauma as an adult. Childhood adversities and adulthood traumas were independently associated with elevated levels of hsCRP (β = 0.03, p = 0.01 and β = 0.05, p < 0.001, respectively). Those who had experienced both types of stress had higher levels of hsCRP than those with adulthood trauma alone, Estimate = −0.06, 95% CI [−0.003, −0.12], p = 0.04, but not compared to those with childhood adversity alone, Estimate = −0.06, 95% CI [0.03, −0.16], p = 0.19. There was no interaction between childhood and adulthood trauma exposure. To our knowledge, this is the first study to examine adulthood trauma exposure and inflammation in a large population-based sample, and the first to explore the interaction of childhood adversity and adulthood trauma with inflammation. Our study demonstrates the prevalence of trauma-related inflammation in the general population and suggests that childhood adversity and adulthood trauma are independently associated with elevated inflammation.

1. Introduction

Exposure to traumatic psychological stress increases risk for psychiatric disorders (Brown et al., 2000; Carr et al., 2013; Turner and Lloyd, 1995) as well as physical morbidity and mortality (Glaesmer et al., 2011; Krause et al., 2004; Shonkoff et al., 2012). Particularly strong evidence links childhood stress exposure with adverse health outcomes. Adversity in childhood increases risk for adult-onset mood and anxiety disorders in the general population, and depression and post-traumatic stress disorder (PTSD) in military personnel (Calabró et al., 2003; Kessler et al., 1997). Childhood adversities also increase risk for physical illnesses including cardiovascular disease, diabetes, and metabolic disorders (Galobardes et al., 2006; Tamayo et al., 2010). Among adults, those with combat or non-combat trauma exposure had an increased rate of psychiatric disorders (Brown et al., 2000; Prigerson et al., 2002) and physical illnesses including heart failure, stroke, and autoimmune disorders (O'Donovan et al., 2015; Spitzer et al., 2009). The biological mechanisms underlying the link between trauma and poor health are not well understood, but there is evidence that inflammation may play a key role (e.g., Danese et al., 2007; O'Donovan et al., 2012).

Emerging evidence indicates that elevated inflammation is associated with psychopathology. Large bodies of research now link depressive and anxiety disorders with elevated levels of inflammation (Howren et al., 2009; O'Donovan et al., 2010, 2013; Toker et al., 2005). PTSD has also been linked with elevated levels

* Corresponding authors at: San Francisco Veterans Affairs Medical Center, 4150 Clement Street (116C-1), University of California, San Francisco, San Francisco, CA 94121, United States.
E-mail addresses: joy.lin@ucsf.edu (J.E. Lin), thomas.neylan@ucsf.edu (T.C. Neylan), elissa.epel@ucsf.edu (E. Epel), aoife.odonovan@ucsf.edu (A. O'Donovan).

http://dx.doi.org/10.1016/j.bbi.2015.11.015
0889-1591/

of inflammatory markers, including C-reactive protein (CRP) (Michopoulos et al., 2015), and higher levels of CRP predicted risk for PTSD symptoms in a prospective study of 2610 war zone-deployed Marines (Eraly et al., 2014). Evidence from animal models and from experimental human research suggests that elevated inflammation is a causal factor that promotes psychiatric symptoms rather than a mere correlate of the disorder (Dantzer et al., 2008; Eisenberger et al., 2010; Raison and Miller, 2013). Chronic low-grade inflammation is also an established risk factor for physical diseases that are associated with trauma exposure, including cardiovascular disease and autoimmune disorders (Harris et al., 1999; Libby, 2002; O'Donovan et al., 2015).

Both childhood adversity and specific types of adulthood trauma exposure have been associated with elevated levels of systemic inflammation. Childhood maltreatment has been linked with elevated levels of high sensitivity C-reactive protein (hsCRP) in participants 20 years later (Danese et al., 2007). Similarly, childhood adversity, defined as having experienced one or more unusually stressful events in childhood, has been associated with elevated adulthood levels of systemic inflammation as well as shorter telomere length (Kiecolt-Glaser et al., 2011; Slopen et al., 2010, 2013). Childhood adversity has also been associated with higher expression of pro-inflammatory genes in a small pilot study (n = 114) of Health and Retirement Study participants (Levine et al., 2015). Across the entire lifespan, greater cumulative exposure to different categories of trauma has also been linked with elevated hsCRP (O'Donovan et al., 2012), as have specific types of adulthood trauma such as being a prisoner of war or a victim of intimate partner violence (Dekaris et al., 1993; Woods et al., 2005). However, in contrast with the large number of studies on childhood adversity and inflammation, there are very few studies that examine the relationship between adulthood trauma exposure and inflammation.

Childhood adversity appears to increase vulnerability to the effects of later stressful events. For example, stress sensitization models hypothesize that childhood adversity may sensitize individuals to psychiatric psychopathology by lowering their tolerance to later stressors (Hammen et al., 2000). One longitudinal study of young women showed that those with a history of childhood adversities were more likely to become depressed following less total stress than women without a similar history, after controlling for previous depression and current chronic stressful conditions (Hammen et al., 2000). Relatedly, adults with a history of childhood adversity or trauma are more likely to develop PTSD following subsequent exposure to adulthood trauma (Breslau et al., 1999; Brewin et al., 2000; Pratchett and Yehuda, 2011). The stress sensitivity associated with childhood trauma may be particularly potent in those with genetic vulnerability; both the *5-HTTLPR* genotype and FKBP5 polymorphisms have been shown to interact with childhood adversity and adulthood trauma to predict adult PTSD (Binder et al., 2008; Xie et al., 2009). While the mechanisms of stress sensitization are unclear, alterations of hypothalamic–pituitary–adrenal (HPA) axis functioning may play a role (Gunnar, 1998, Heim and Nemeroff, 2001; Miller et al., 2011). For instance, early life stress has been shown to induce sensitization of corticotropin-releasing factor (Heim and Nemeroff, 2001). This sensitization is associated with pro-inflammatory tendencies that may be exacerbated by behavioral proclivities such as hypervigilance, poor social relationships, and adverse health behaviors, which are themselves associated with childhood adversity (Miller et al., 2011). To our knowledge, no population-based studies have examined whether people who have experienced childhood adversity are more susceptible to inflammation associated with adulthood trauma exposure.

In the present study, we examine whether exposure to childhood adversity, adulthood trauma, and their interaction are associated with elevated inflammation in a large population-based sample of Americans over the age of 50. Advantages of a population-based study were that they allowed for estimation of the distribution and prevalence of childhood adversity and adulthood trauma, minimization of confounders to exposures and outcomes, and maximization of external validity and generalizability. We analyzed both the presence and the number of childhood adversities and adulthood traumas, because the number of adverse experiences can increase risk for inflammation and for the development of physical and mental disorders (Coker et al., 2005; McLaughlin et al., 2010; O'Donovan et al., 2012). We also considered the contribution of health behaviors, as both childhood trauma and specific types of adulthood trauma have been associated with smoking, alcohol use, obesity, and physical and mental health conditions (Dube et al., 2003; Kaysen et al., 2007; Kessler et al., 1997; Pizarro et al., 2006; Vieweg et al., 2007; Williamson et al., 2002). These health behaviors have in turn been linked to elevated inflammation (O'Connor and Irwin, 2010). Inflammation was measured using hsCRP, an acute-phase reactant and nonspecific marker of inflammation that is secreted by the liver and adipose tissues (Libby, 2002). Current evidence supports the use of hs-CRP as the analyte of choice for systemic inflammation, after considering the various analytes' stabilities; the analytes' assay precision, accuracy, and availability; and the availability of standards for proper assay calibration (Pearson et al., 2003). Given prior research linking childhood adversity and adulthood trauma to elevated systemic inflammation, we predicted that exposure to childhood adversity and adulthood trauma would independently be associated with higher levels of hsCRP. As previous studies suggest that childhood adversity may increase vulnerability to adulthood stressors through HPA axis sensitization and pro-inflammatory activity, we aimed to assess the relative contribution of childhood adversity and adulthood trauma to inflammation by assigning study members to 1 of 4 groups as follows: no history of childhood adversity or adulthood trauma; history of childhood adversity but no adulthood trauma; no history of childhood adversity but history of adulthood trauma; history of both childhood adversity and adulthood trauma. We hypothesized that those with a history of both childhood adversity and adulthood trauma would have elevated levels of inflammation compared to those with a history of childhood adversity or adulthood trauma alone. Those with neither a history childhood adversity nor adulthood trauma would have the lowest levels of inflammation. We further predicted that there would be a significant interaction between the two types of stress.

2. Methods

2.1. Participants

Participants were drawn from the Health and Retirement Study (HRS), a longitudinal study of a population-based sample of more than 20,000 Americans over the age of 50. The target population for the original HRS cohort includes all adults in the contiguous United States born during the years 1931–1941 who reside in households, with a 2:1 oversample of African-American and Hispanic populations. The original sample has been refreshed with new birth cohorts over the years. Starting in 2006, the study implemented a psychosocial questionnaire that included assessments of childhood adversity and adulthood trauma (Clarke et al., 2008). In the same year, the study also implemented biomarker assessments (Crimmins et al., 2013), which were completed by half of the participants in 2006, and half of the participants in 2008. For our analyses, we used the combined data from 2006 and 2008. We selected participants from the original sample who had (1) completed the measures for either childhood adversity or adulthood trauma,