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Race/ethnicity moderates the relationship between depressive symptom severity and C-reactive protein: 2005–2010 NHANES data

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ABSTRACT

Because few studies have examined depression facets or potential moderators of the depression–inflammation relationship, our aims were to determine whether particular depressive symptom clusters are more strongly associated with C-reactive protein (CRP) levels and whether race/ethnicity moderates these relationships. We examined data from 10,149 adults representative of the U.S. population (4858 non-Hispanic White, 1978 non-Hispanic Black, 2260 Mexican American, 1053 Other Hispanic) who participated in the cross-sectional National Health and Nutrition Examination Survey between 2005 and 2010. Depressive symptoms were assessed by the Patient Health Questionnaire-9, and high-sensitivity serum CRP was quantified by latex-enhanced nephelometry. Total ($p < .001$), somatic ($p < .001$), and nonsomatic ($p = .001$) depressive symptoms were each positively related to serum CRP in individual models. However, in the simultaneous model that included both symptom clusters, somatic symptoms ($p < .001$), but not nonsomatic symptoms ($p = .98$), remained associated with serum CRP. Evidence of moderation by race/ethnicity was also observed, as six of the nine depressive symptoms × race/ethnicity interactions were significant ($ps < .05$). Among non-Hispanic Whites, the pattern of results was identical to the full sample; only somatic symptoms ($p < .001$) remained related to serum CRP in the simultaneous model. No relationships between total, somatic, or nonsomatic symptoms and serum CRP were observed among the non-Hispanic Black, Mexican American, or Other Hispanic groups. Our findings indicate that the link between depressive symptoms and systemic inflammation may be due to the somatic symptoms of sleep disturbance, fatigue, appetite changes, and psychomotor retardation/agitation and may be strongest among non-Hispanic Whites.

1. Introduction

Considerable evidence suggests that depression is an independent risk factor for atherosclerotic cardiovascular disease (CVD), including coronary artery disease and cerebrovascular disease (Van der Kooy et al., 2007). The longitudinal relationship between depression and incident CVD is consistent, as it has been observed in both genders and in various age and racial/ethnic groups (Rosengren et al., 2004; Van der Kooy et al., 2007). Because depression is a multidimensional construct or disorder composed of affective, cognitive, behavioral, and somatic symptoms (Davidson et al., 2005), recent investigations have compared the relative importance of these symptom clusters in predicting CVD risk. Findings of these studies have been contradictory; some investigators have reported that the somatic symptoms are stronger predictors of CVD risk markers or outcomes (Deverts et al., 2010; Stewart et al., 2007, 2009), whereas others have observed similar results for the affective and cognitive symptoms (Everson et al., 1996; Kubzansky et al., 2001; Matthews et al., 2004; Stewart et al., 2012). Consequently, whether or not certain depressive symptoms clusters are more cardiotoxic than others remains an open question.

Systemic inflammation is one mechanism that might explain how depression promotes the development of CVD (Kop and Gottdiener, 2005). A recent meta-analysis revealed that various inflammatory markers – i.e., the proinflammatory cytokines, interleukin (IL)-1 and IL-6, and the acute phase reactant, C-reactive protein (CRP) – are upregulated in individuals with depressive disorders or elevated symptoms, although substantial heterogeneity was observed across studies (Howren et al., 2009). In addition, some investigations (Boyle et al., 2007; Stewart et al., 2009), but not all (Gimeno et al., 2009; Kiecolt-Glaser et al., 2003), have found

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that depression predicts increases in inflammatory marker levels over periods of up to 10 years. Notably, systemic inflammation is thought to play a role in all phases of atherosclerosis (Epstein and Ross, 1999), and several of the inflammatory markers elevated in depression, such as CRP, are predictive of incident CVD after adjustment for conventional cardiovascular risk factors (Kaptoge et al., 2012).

Despite the substantial literature on the depression–inflammation relationship, only four studies have examined whether the strength of this association varies across depressive symptom clusters. In a sample of 263 healthy, older adults most of whom were non-Hispanic White, we found that the somatic-vegetative symptoms of depression, but not cognitive-affective symptoms, predicted increases in IL-6 over six years (Stewart et al., 2009). Neither symptom cluster, however, predicted 6-year change in CRP. In a sample of 2544 healthy, middle-aged adults over 40% of whom were non-Hispanic Black, Deverts et al. (2010) observed that race moderated the prospective association between depressive symptoms and CRP. Among non-Hispanic Blacks, the somatic and positive affect subscales of the depression measure, but not depressed affect and interpersonal problems subscales, were independent predictors of 5-year increases in CRP. In contrast, none of the symptom clusters predicted change in CRP among non-Hispanic Whites. In a population-based sample of 5000 adults aged 35–74 years, Michal and colleagues (2013) found that only somatic depressive symptoms were cross-sectionally associated with various inflammatory markers, including CRP, in age- and sex-adjusted analyses. These relationships, however, did not persist after further adjustment for traditional CVD risk factors. Finally, Duivis et al. (2013) recently reported that, after adjustment for demographic and health factors, the somatic but not the cognitive symptoms were positively related to CRP, IL-6, and tumor necrosis factor-α levels in 2861 Dutch community members aged 18–65 years. Collectively, the available results suggest that the somatic symptoms may be more strongly related to systemic inflammation than other depressive symptom clusters; however, the small number of studies still renders this a tenuous conclusion. In addition, the intriguing findings of Deverts et al. (2010) highlight the need for additional studies examining race/ethnicity as a potential moderator of the depression–inflammation relationship.

Accordingly, the aims of the present study were (1) to determine whether particular depressive symptom clusters are more strongly associated with serum CRP, a nonspecific marker of systemic inflammation predictive of incident CVD (Pearson et al., 2003), and (2) to test whether race/ethnicity is a moderator of the depression–CRP relationship. To achieve these aims, we examined data from a large sample of adults, representative of the U.S. population, who participated in cross-sectional National Health and Nutrition Examination Survey (NHANES) between 2005 and 2010. These survey years provided a good opportunity to accomplish our aims because most of the respondents completed a multidimensional measure of depressive symptoms and underwent a blood draw to quantify high-sensitivity serum CRP. Furthermore, the 2005–2010 sample consists of large numbers of individuals of African American and Latino descent.

2. Methods

2.1. Study design and sample

We examined cross-sectional data from the 2005–2010 NHANES survey years. These data were collected by the National Center for Health Statistics of the Centers for Disease Control and Prevention from a nationally representative sample of civilian, non-institutionalized adults and children to assess the health and nutritional status of the U.S. population. Detailed descriptions of the survey design (a stratified, multistage, probability sample) and procedures are available at the study website (www.cdc.gov/nchs/nhanes.htm). Briefly, approximately 5000 people were recruited each survey year, and non-Hispanic Blacks and Hispanics were among the groups oversampled to ensure accurate estimates. Individuals who were selected and agreed to participate completed a computer-assisted interview conducted by trained personnel in their homes. Additional interviews (including the depressive symptoms assessment) and all examinations (including the blood draw) were conducted at Mobile Examination Centers (MEC) after the home interview. This archival study was approved by the institutional review board at Indiana University-Purdue University Indianapolis.

From the total sample for the 2005–2010 survey years ($N = 31,034$), we selected all respondents aged 18 years and older ($n = 18,318$), of whom 15,136 had complete data for CRP and answered eight or more of the nine depression items. We then excluded 3397 adults who reported a history of one or more of the following conditions due to their likely influence on CRP levels: cardiovascular disease (coronary heart disease, angina, myocardial infarction, stroke, or congestive heart failure) (Casas et al., 2008; Pearson et al., 2003), chronic bronchitis (Gan et al., 2004), emphysema (Omori et al., 2009), rheumatoid arthritis (Sokka and Pincus, 2009), human immunodeficiency virus (Tien et al., 2010), hepatitis C (Kessel et al., 2007), liver conditions (Tilg et al., 1992), and kidney conditions (Abraham et al., 2009). Next, we excluded 1043 adults with CRP levels $\geqslant$10 mg/L, as values above this cut point are likely due to acute infection, trauma, or another non-cardiovascular cause (Pearson et al., 2003). Finally, we excluded the 547 respondents in the Other Race group (see Section 2.2.3 below). Thus, our final sample consisted of 10,149 adults (see Table 1 for characteristics).

2.2. Measures and procedures

2.2.1. Depressive symptoms

The Patient Health Questionnaire (PHQ-9) (Kroenke et al., 2001) was administered during the MEC examination to assess depressive symptom severity during the past two weeks. Using a 4-point scale (0 = not at all, 1 = several days, 2 = more than half the days, 3 = nearly every day), respondents indicated the frequency with which they had experienced the following nine symptoms of major depressive disorder: (1) anhedonia, (2) depressed mood, (3) sleep disturbance, (4) fatigue, (5) appetite changes, (6) low self-esteem, (7) concentration problems, (8) psychomotor retardation/agitation, and (9) suicidal ideation. Total scores range from 0 to 27, with scores $\geqslant$10 being indicative of clinically significant depressive symptoms (Kroenke and Spitzer, 2002). The PHQ-9 has been shown to be a reliable and valid questionnaire in community samples, as indicated by its high internal consistency and good sensitivity and specificity for identifying cases of major depressive disorder (Kroenke and Spitzer, 2002; Kroenke et al., 2001; Manea et al., 2012; Patten and Schopflocher, 2009; Wittkampf et al., 2007).

For 70 respondents missing one PHQ-9 item, we imputed the missing value using the mean of the other eight items for that individual. We then calculated PHQ-9 Total (sum of all items) and two subscale scores. The PHQ-9 Somatic subscale score was computed by summing the sleep disturbance, fatigue, appetite changes, and psychomotor retardation/agitation items (Items 3, 4, 5, and 8), and the PHQ-9 Nonsomatic subscale score was computed by summing the remaining five items (Items 1, 2, 6, 7, and 9). Although prior studies have reported support for a one-factor model with all nine items loading on a single depression factor (Cameron et al., 2011; Huang et al., 2006), recent confirmatory factor analyses have found that a two-factor model provided a better fit to the

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