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Depression inhibits the anti-inflammatory effects of leisure time physical activity and light to moderate alcohol consumption

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ABSTRACT

Light to moderate alcohol consumption and leisure time physical activity (LTPA) are independently associated with lower levels of high sensitivity C-reactive protein (CRP), a predictor of cardiometabolic risk. In contrast, depression, ranging from low mood disturbance to major depressive disorder, has been associated with elevated CRP. To test the hypothesis that depression attenuates the anti-inflammatory effects of LTPA and alcohol consumption, the current study tested the moderating effect of severity of depressive symptomatology on the relation of alcohol consumption and LTPA to CRP in 222 healthy adult men and women (18–65 years of age). Given the known effects of gender on inflammation, we also examined the effects of gender on the tested interactions. Depression was assessed using the Beck Depression Inventory. Frequency of alcohol consumption, hours of LTPA per week and other coronary risk/protective factors were assessed via self-report and structured interview. Fasting blood samples were used to measure CRP and lipids. As predicted, the interaction between LTPA and depressive symptomatology was significant ($F = 5.29$, $p < .03$) such that lower CRP was associated with the combination of decreased depressive symptomatology and increased LTPA. Among those with increased depressive symptoms, increased LTPA was not associated with higher CRP. Similarly, depression interacted with alcohol consumption in predicting CRP in men but not women ($F = 5.03$, $p < .008$) such that for men light to moderate alcohol consumption was associated with lower CRP but only among those with decreased depressive symptoms. Light to moderate alcohol consumption was not associated with lower CRP in those with increased depressive symptom severity. The pattern of the interactions between anti-inflammatory activities such as light to moderate alcohol consumption and LTPA and psychological distress as indexed by severity of depressive symptomatology suggests an important new avenue for future research.

1. Introduction

Lifestyle factors such as leisure time physical activity (LTPA) and light-to-moderate alcohol consumption are associated with lower risk of cardiovascular disease (CVD) and type 2 diabetes (T2D) (Blair et al., 1989; Brien et al., 2011; Dunkley et al., 2012; Fagard, 1993; Golbidi and Laher, 2012; Joosten et al., 2010; Kelley et al., 2012a,b; Lee and Skerrett, 2001; Oguma and Shinoda-Tagawa, 2004; Okada et al., 2010; Paffenbarger et al., 1986; Pietraszek et al., 2010; Ronksley et al., 2011; Umpierre et al., 2011). It is believed that the benefits of LTPA and moderate alcohol consumption on reducing risk reflect improvements in cardiometabolic risk factors. Thus, LTPA and moderate alcohol consumption have been associated with lower blood pressure (Fagard, 1993), improved lipid and lipoprotein profile (Brien et al., 2011; Kelley et al., 2012a), reduced coagulation and platelet aggregation (Brien et al., 2011) and improved insulin sensitivity (Pietraszek et al., 2010).

Researchers have shown that LTPA and alcohol consumption also reduce inflammation. In cross-sectional, longitudinal and experimental studies, LTPA (Kasapis and Thompson, 2005; Panagiotakos et al., 2005) and moderate alcohol consumption (i.e., 1–2 drinks/day) are associated with lower levels of high-sensitivity C-reactive protein (hsCRP) (Kelley and Kelley, 2006; Michigan et al., 2011; Raum et al., 2007), an acute-phase protein that predicts future risk of CVD (Ridker, 2001; Ridker et al., 1998; Ridker et al., 2000; Zairis et al., 2004) and T2D (Han et al., 2002; Thorand et al., 2007). While CRP is a non-specific marker of inflammation (Saito et al., 2003), evidence suggests that it plays an active role in the pathogenesis of atherosclerotic plaque formation (Du Clos, 2000; Ishikawa et al., 2004) through its facilitation of low density lipoprotein (LDL) cholesterol absorption (Zwaka et al., 2001), recruitment of monocytes to arterial wall (Pasceri et al., 2000) and reduction of vasoreactivity (Silva and Pais de Lacerda, 2012). Such effects have led some to suggest that CRP is not only a

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surrogate biomarker for disease risk but also a mediator in disease pathophysiology (Verma and Yeh, 2003).

In contrast to the beneficial effects of LTPA and moderate alcohol consumption, depression and its defining symptoms are prospectively associated with an increased risk of both CVD (Khan et al., 2010; Lippi et al., 2009; Nemeroff and Goldschmidt-Clermont, 2012) and T2D (Brown et al., 2005; Carnethon et al., 2007). Evidence suggests that depression increases the risk of CVD by 50–100%, and also worsens the outcome for patients who experience a cardiac event (Lippi et al., 2009). Similarly, depression increases the risk of T2D by 60% (Mezuk et al., 2008). While underlying mechanisms have not been well elucidated, a number of studies have reported that depression, ranging from low mood to major depressive disorder, is associated with higher levels of inflammatory biomarkers including hsCRP (Davidson et al., 2009; Elovainio et al., 2009; Ferketich et al., 2005; Lindqvist et al., 2009; Musselman et al., 2001; Pikhart et al., 2009; Suarez, 2004; Suarez and Boyle, 2005).

The link between depression and disease outcomes has been extensively explored with a number of studies examining putative physiological mechanisms linking depression and disease endpoints (Rozanski et al., 1999). For the most part, the primary approach employed by studies that examine putative mechanisms emphasizes the direct effect of depression on plausible mechanisms and subsequent clinical outcomes. While this approach has yielded a wealth of evidence for the role of depression in onset and progression of various clinical conditions (Herbert and Cohen, 1993; Howren et al., 2009), it is reasonable to speculate that the impact of depression may also include inhibition of beneficial effects associated with risk-reducing activities. In other words, depression may act as a rate-limiting factor that inhibits or attenuates the cardioprotective effects of activities known to lower the risk of CVD and T2D such as LTPA and moderate alcohol consumption. Such an approach may reveal that depression, and more broadly psychological distress, not only has direct effects on putative mechanisms but also indirect effects that are characterized by diminished improvements in traditional and emerging risk factors following health promoting activities.

Recently, two studies have assessed the moderating effects of indicators of psychological distress on the relation of physical activity to immune responses to influenza vaccination. For example, Segerstrom et al. (2012) showed that higher levels of psychological distress, a latent construct that incorporated items from the Geriatric depression scale, attenuated antibody responses to vaccinations in persons who were physically active. In contrast, a more robust antibody response to vaccination was observed in subjects who were physically activity and reported low levels of psychological distress (Segerstrom et al., 2012). Similarly, Emeny et al. also examined the interaction between psychological distress as indexed by level of job strain and physical activity on CRP (Emeny et al., 2012). Emeny et al. showed that the beneficial effects of physical activity on reducing CRP were absent in people reporting high job strain but present in people with low job strain (Emeny et al., 2012). While preliminary, these findings support the general hypothesis that markers of psychological distress may act to inhibit or diminish the anti-inflammatory or immunological responses to health promoting behaviors. In contrast, the positive consequences of health promoting behaviors would be more likely to be observed among those with lower psychological distress. In testing this general hypothesis, the present study examined the moderating effect of psychological distress, as indexed by severity of depressive symptoms, on the relation of LTPA and alcohol consumption to hsCRP.

To fully explore the hypothesized interactions, we also examined the role of gender. Previous reports have shown that gender moderates the health-related effects of ethanol (Albert et al., 2003; Greenfield et al., 2002; Oliveira et al., 2010). It is also acknowledged that the prevalence of depression differs between men and women. Combined, these observations raise the possibility that gender may moderate the joint effect of depression and alcohol consumption on CRP. To test this possibility, we examined the three-way interaction between gender, alcohol use and depression as well as the three-way interaction between gender, LTPA and depression.

2. Methods

2.1. Participants

Participants were 222 nonsmoking healthy men and women between the ages of 18 and 65 years. Subjects were enrolled in studies examining the relation of inflammatory biomarkers (e.g., C-reactive protein) to psychosocial risk factors of cardiovascular disease (Suarez, 2004). Subjects were recruited from the general community via advertisements placed in newspapers, online websites and fliers distributed throughout the community. Interested individuals were screened for entry criteria using a self-report health questionnaire and interview. Inclusion criteria included the following: no history or current diagnosis of psychiatric conditions; no current or previous use of anti-depressant medications; and no chronic medical conditions related to inflammation, such as asthma, allergies, arthritis, diabetes, all forms of cancer and cardiovascular diseases including hypertension. Women who used oral contraceptives or hormone replacement therapy were excluded.

2.2. Assessments

2.2.1. Depression

The 21-item Beck depression inventory (BDI) was used to assess symptoms of depression for the two weeks prior to administration (Beck et al., 1988). Subjects were instructed to respond to each item (e.g., "I often feel sad.") using a four-point scale ranging from 0 (symptom not present) to 3 (symptom very intense) with total score ranging from 0 to 63. The depressive symptoms characterized were negative mood, sadness, pessimism, decreased functioning (e.g., indecisiveness), work inhibition, and somatic problems (e.g., insomnia and fatigue) (Beck et al., 1988). The BDI was administered on the day that blood samples were collected. While the BDI is not designed to yield a clinical diagnosis, scores are significantly correlated with a diagnosis of major depressive disorder (Beck et al., 1988). A previous study using the BDI to screen for depression in a general population reported that, of 1240 subjects between the ages of 18 and 64, 4.16% scored 13 and above on the BDI, a cut-off point with 100% sensitivity, 99% specificity and 98% overall diagnostic value for depressive disorder (Lasa et al., 2000). In our sample, 4.5% scored 13 and above, with none of these subjects having been previously diagnosed with major depressive disorder. Due to the skewness of the distribution, BDI was log-transformed and used as a continuous variable in all analysis.

2.2.2. Alcohol consumption

Alcohol consumption was classified according to the scheme used by Albert et al. (Albert et al., 2003): never/former (<1 drink in past 12-months), infrequently (1–3 drinks/month), occasionally (1–7 drinks/week), and regularly (2 or more drinks/day). Due to the low number of subjects in the "regular" category (men: 9.9%; women: 6.6%), we combined the categories of "occasionally" and "regularly." Combining these two categories resulted in a subgroup where women reported drinking an average of ½ drink/day (median = 0.43 drinks/day, IQ range: 0.29–1.14) and men drinking

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