Short Communication

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Isolation associations of exercise intensity on inflammation: Does engaging in moderate or vigorous intensity exercise in isolation have an influence on inflammation?

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ABSTRACT

Objective: The purpose of this study was to examine whether engaging in certain physical activity intensity levels in isolation (e.g., only vigorous exercise) are associated with the C-reactive protein (CRP). **Methods:** Data were extracted from the 1999 to 2006 National Health and Nutrition Examination Survey (7564 adults; 18-50 years). CRP was assessed from a blood sample and participants reported whether or not they engaged in moderate-intensity physical activity (MPA), vigorous-intensity physical activity (VPA), or moderate-to-VPA (MVPA). **Results:** After adjusting for age, gender, race-ethnicity, and body mass index, when compared to those who engaged in MVPA, those who engaged in only MPA ($\beta_{adjusted} = 0.08$; 95% confidence interval [CI]: 0.04-0.12; $P < 0.001$) had higher CRP levels. After adjustments, when compared to those who engaged in only VPA, those who engaged in only MPA ($\beta_{adjusted} = 0.06$; 95% CI: 0.001-0.11; $P = 0.04$) had higher CRP levels. Finally, after adjustments, there was no difference between those who engaged in only VPA ($\beta_{adjusted} = 0.02$; 95% CI: −0.03-0.07; $P = 0.45$) compared to those engaging in MVPA. **Conclusion:** These findings suggest that, among those reporting engagement in physical activity, those who exclusively limit their engagement to MPA may have worse health outcomes associated with higher CRP when compared to those engaging in VPA and MVPA.

KEY WORDS: Behavior, epidemiology, inflammation, isolation

INTRODUCTION

Elevated C-reactive protein (CRP) is indicative of increased systemic inflammation, with increased systemic inflammation facilitating the development and progression of diabetes [1], cardiovascular disease [2], chronic kidney disease [3], and various mental health disorders [4]. Previous research demonstrates that both moderate-intensity physical activity (MPA) and vigorous-intensity physical activity (VPA) are associated with various health outcomes (e.g., cardiovascular disease) [5], with moderate-to-VPA (MVPA) being inversely associated with CRP [6]. However, to our knowledge, the isolation effect of physical activity intensity on health [7], let alone CRP, is relatively unknown. Therefore, the purpose of this short communication was to examine whether engaging in certain physical activity intensity levels in isolation (e.g., only vigorous exercise) are associated with CRP. We hypothesize that behavioral isolation, compared to engaging in behaviors of multiple intensities, will have a less favorable effect on inflammation (i.e., higher CRP). Specifically, the following questions were of interest in this study. Among those who self-report engagement in physical activity:

1. Did those who report only engaging in MPA have higher CRP levels when compared to those engaging in MVPA?
2. Did those who report only engaging in MPA have higher CRP levels when compared to those engaging in VPA?
3. Did those who report only engaging in VPA have higher CRP levels when compared to those engaging in MVPA?

METHODS

Design and Participants

Data were extracted from the 1999 to 2006 National Health and Nutrition Examination Survey (NHANES); these are the only NHANES cycles with identical measures of the assessed self-reported physical activity intensity variables. The NHANES is an ongoing survey conducted by the Centers for Disease Control and Prevention that uses a representative sample of non-institutionalized United States civilians selected by a complex, multistage, stratified, clustered probability design. Procedures were approved by the National Center for Health Statistics

review board. Consent was obtained from all participants before data collection.

In the 1999-2006 NHANES cycles, 22,624 adults (≥18 years) participants enrolled. After excluding those with missing self-reported physical activity data, 21,392 remained. After excluding those with missing CRP or covariate data (i.e., age, gender, race-ethnicity, or measured body mass index), 18,633 remained.

Among these 18,633 adults, 5204 reported engaging in only MPA; 2132 reported engaging in only VPA; and 3965 reported engaging in both MPA and VPA (i.e., MVPA). Among these, the mean sample age was much higher for those engaging in only MPA (48.7 years), compared to those engaging in only VPA (37.2 years) or MVPA (36.8 years). When excluding those above 50 years of age, the mean sample age was similar across the groups: Only MPA (32.7 years; $n = 2803$), only VPA (29.5 years; $n = 1659$), and MVPA (29.8 years; $n = 3102$).

The final analytic sample included these 7564 adults 18-50 years (2803 for only MPA; 1659 for only VPA; and 3102 for MVPA). Thus, only participants reporting engagement in physical activity were included in the analysis (justified in the discussion section). It was also of interest to create groups of similar ages to minimize any age effects of the relationship between physical activity isolation and CRP.

Physical Activity

For MPA, participants were asked: "*Over the past 30 days, did you do moderate activities for at least 10 min that cause only light sweating or a slight to moderate increase in breathing or heart rate?*" (Yes/no response).

For VPA, participants were asked: "*Over the past 30 days, did you do vigorous activities for at least 10 min that caused heavy sweating, or large increases in breathing or heart rate?*" (Yes/no response).

As noted above, from these two items, three groups were created: (1) Those only engaging in MPA (answering "yes" to the MPA variable and "no" to the VPA variable), (2) those only engaging in VPA (answering "yes" to the VPA variable and "no" to the MPA variable), and (3) those engaging in both MPA and VPA (i.e., MVPA).

CRP

Blood samples were obtained to assess high sensitivity CRP, using latex-enhanced nephelometry. The coefficients of variation ranged from 3.1% to 9.9%.

Analysis

Statistical analyses were performed via procedures from survey data using Stata (v.12). To account for oversampling, non-response, non-coverage, and to provide nationally representative estimates, all analyses included the use of survey sample weights, clustering, and primary sampling units. Multivariable linear regression analysis was used to examine the association between the three isolation groups and CRP (outcome variable). Covariates included age, gender, race-ethnicity, and body mass index. Notably, when including additional covariates in the models such as diabetes, coronary artery disease, and cancer, results were unchanged (data not shown). Statistical significance was established as two-sided $P < 0.05$.

RESULTS

Among the groups of only MPA, only VPA, and MVPA, the proportion, in which men were 35.6%, 60.8%, and 54.0%, respectively. Among these three groups, the proportion, in which non-Hispanic white were 49.3%, 37.3%, and 49.5%, respectively. Among these three groups, the mean (95% confidence interval [CI]) body mass index (kg/m^2) was 28.5 kg/m^2 (28.2-28.7), 27.1 kg/m^2 (26.7-27.3), and 26.9 kg/m^2 (26.6-27.0), respectively. Among these three groups, the mean (95% CI) CRP (mg/dL) was 0.49 mg/dL (0.46-0.52), 0.30 mg/dL (0.27-0.33), and 0.31 mg/dL (0.28-0.33), respectively.

The three specific questions and their associated results are as follows:

1. Did those who report only engaging in MPA have higher CRP levels when compared to those engaging in MVPA?
   In a multivariable linear regression adjusting for age, gender, race-ethnicity, and body mass index, when compared to those who engaged in MVPA, those who engaged in only MPA ($\beta_{adjusted} = 0.08$; 95% CI: 0.04-0.12; $P < 0.001$) had higher CRP levels.
2. Did those who report only engaging in MPA have higher CRP levels when compared to those engaging in VPA?
   In a multivariable linear regression adjusting for age, gender, race-ethnicity, and body mass index, when compared to those who engaged in VPA, those who engaged in only MPA ($\beta_{adjusted} = 0.06$; 95% CI: 0.001-0.11; $P = 0.04$) had higher CRP levels.
3. Did those who report only engaging in VPA have higher CRP levels when compared to those engaging in MVPA?
   In a multivariable linear regression adjusting for age, gender, race-ethnicity, and body mass index, there was no difference between those who engaged in only VPA ($\beta_{adjusted} = 0.02$; 95% CI: −0.03-0.07; $P = 0.45$) compared to those engaging in MVPA.

Notably, for all models, results were similar for unadjusted estimates (data not shown). Although slight differences were observed for the univariate analyses (first paragraph of the results section), the similar unadjusted and adjusted regression results suggest that the observed association between physical activity isolation and CRP was not driven by body mass index or the evaluated demographic parameters.

DISCUSSION

Research continues to demonstrate beneficial effects of physical activity duration [8], along with favorable intensity-related

effects of MPA, VPA, and MVPA [5,9] with some evidence to suggest greater benefits associated with VPA compared to MPA [10-12]. Although research has examined independent effects of physical activity intensity, as well as domain-specific physical activity (e.g., leisure time vs. occupational) [10,13] to our knowledge, no studies have specifically examined the effects of isolated physical activity on inflammation. As such, the purpose of this short communication was to examine the isolated associations of MPA, VPA, and MVPA on CRP.

In this study, it was not in our interest to make comparisons to those who reported no engagement in physical activity, as it is well established that those who are less active have worse health outcomes when compared to those who are active. As a result, the analyses exclusively focused on three groups: Those only engaging in MPA, those only engaging in VPA, and those engaging in MVPA. The main findings from these analyses were two-fold: (1) Those who only engaged in MPA had higher CRP levels when compared to those engaging in only VPA or both MPA and VPA (i.e., MVPA) and (2) similar CRP levels were observed between those engaging in only VPA and those engaging in MVPA. These findings suggest that, among those reporting engagement in physical activity, those who exclusively limit their engagement to MPA may have worse health outcomes associated with higher CRP when compared to those engaging in VPA or MVPA. If future research confirms these findings, then mechanistic studies examining underlying mechanisms to explain these findings is warranted. It is possible that this intensity-specific effect is influenced by total physical activity volume, which warrants further investigation. However, there may also be unique intensity-specific adaptations. For example, research has demonstrated greater cardiorespiratory fitness adaptations in high-intensity training when compared to continuous moderate-intensity training [14]. Further, the endothelial function has been shown to improve to a greater extent following higher-intensity training when compared to continuous moderate-intensity training [14]. This intensity-specific effect is in alignment with our previous work showing that VPA was the only isolated intensity associated with reduced premature all-cause mortality [7]. Taken together, this suggests that the protective habitual effects of VPA on mortality and other health outcomes may be a result of the habitual effects of VPA on systemic inflammation [15].

Owing to the limitations of the MPA and VPA items, it was not possible to determine the duration and frequency of these physical activity parameters, but rather whether they engaged in the intensity level or not. Future studies examining the extent to which isolated MPA/VPA duration and frequency influence health are warranted. We also acknowledge that "acute" VPA may induce a pro-inflammatory response, with "chronic" VPA having an anti-inflammatory response [16]. Given that the physical activity questions were in reference to the last 30 days, coupled with the current findings of an inverse association between VPA and CRP, it may be reasonable to assume that the present findings are in alignment with an anti-inflammatory effect of VPA. Like most epidemiological studies, another limitation is the potential of residual and unmeasured confounding. Further, the cross-sectional study design precluded the ability to establish temporal sequence, and as such, we cannot discount the potential of reverse causality. Despite these limitations, major strengths of this study include the national sample employed as well as the study's novelty. If these findings are confirmed by future research, then while attempting to promote engagement in MVPA, specific attention should be focused on the promotion of both MPA and VPA.

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