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Meeting Physical Activity Guidelines Is Associated with Lower Allostatic Load and Inflammation in Mexican Americans

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Introduction

Allostatic load refers to the accumulation of physiologic risk factors for chronic disease due to exposure to psychological stressors.(1) Repetitive stress causes dysregulation of the neuroendocrine system and subsequent elevation in inflammatory markers, leading to metabolic syndrome and chronic diseases such as cardiovascular disease. Allostatic load is commonly assessed by panels of biomarkers that include indicators like C-reactive Protein, cortisol levels, glycosylated hemoglobin, BMI, and blood pressure.(2)

It is possible that regular physical activity counters accumulation of allostatic load.(3) Increases in physical activity are linked to decreases in psychosocial stress, resulting in lowered cortisol, reactivity of the HPA axis (4), and thereby reducing accumulation of allostatic load. Also, physical activity clearly reduces risk of metabolic syndrome, an important factor in blood pressure control, and is associated with lower levels of inflammatory markers such as C-reactive protein.(5-7) These risk factors are representative of the physiologic dysregulation that results from increased stress (i.e., metabolism, cardiovascular function, and immune system).(2) Although associations between physical activity and allostatic load components are evident, there is a paucity of evidence linking physical activity with allostatic load beyond theoretical support.(8)

Of particular interest is whether physical activity deters accumulation of allostatic load in Mexican Americans. Accelerometry measures of physical activity suggest Mexican Americans are the most physically active ethnic group—more active than non-Hispanic

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whites and blacks.(9, 10) Increased participation in physical activity among Mexican Americans may explain observed patterns of improved health outcomes relative to non-Hispanic whites. Could allostatic load partially explain the so-called “Hispanic paradox” of lower age-adjusted mortality rates in Mexican Americans? So far, little is known about how physical activity influences allostatic load in Mexican-Americans. Two studies report that foreign-born Mexican American adults have lower allostatic scores than US-born Mexican-Americans, but did not examine if physical activity levels could explain the differences.(11, 12) Gallo et al. reported no association between physical activity and allostatic load scores among middle-aged Mexican American women, and the study did not include men.(12)

In an effort to evaluate the potential association between physical activity and allostatic load, this study examined whether a dose-response relation existed between allostatic load and level of physical activity in a cohort of Mexican American adults. It is anticipated that higher levels of physical activity participation will be related to lower levels of metabolic, blood pressure and inflammatory risk, as well as lower total allostatic load. Tests of whether the associations between physical activity and allostatic load varied by age, sex, and education level were also examined due to the known associations between these factors with physical activity and health outcomes. It was hypothesized that the relationship between physical activity with risk factors and total allostatic load would vary by established correlates of physical activity including sex, age, education.(13) Age is also positively associated with allostatic load accumulation (14), warranting inclusion as a covariate.

Methods

Participants

This study uses data collected as part of the Cameron County Hispanic Cohort (CCHC).(15) In brief, the study recruited Mexican-Americans from the first and third income census block quartiles in Cameron county—a county on the US-Mexico border. Households were sampled, and all adults in the household aged 18 years and older were invited to participate. All protocols and data collection for the CCHC was approved by an Institutional Review Board. Of the 2,000 enrolled participants from the CCHC, 368 were randomly selected for additional measures of inflammatory markers (cytokine and adipokine assays) in 2008 to 2010. The sample for the present study is 330 of these 368 participants, who had complete data on physical activity levels. Analyses were conducted in 2011.

Data Collection

Data collected on all participants of the CCHC included: blood pressure, heart rate, anthropometric measures, fasting blood glucose, glycosylated hemoglobin, lipid panel, and C-reactive protein. Participants were asked to self-report the highest level of education attained, age in years, sex, country of birth, and the number of years they have lived in the county. Each participant completed a medical history and health behavior questionnaire that provided information on physical activity behavior. More information on the methods used in the CCHC has been published.(15) Procedures and instruments were approved by the Committee for the Protection of Human Subjects, and written informed consent collected prior to data collection.

Physical Activity—Data on physical activity were collected through interviewer-administered questionnaire in the language selected by the participant (Spanish or English). Physical activity was assessed using the International Physical Activity Questionnaire short-form (IPAQ).(16) The IPAQ assesses self-reported physical activity for sitting time, walking, moderate-, and vigorous-intensity physical activity. The IPAQ possesses acceptable criterion validity with objectively measured physical activity (16) and fitness.(17) Using the IPAQ protocol, physical activity was calculated as minutes per week multiplied by metabolic equivalent values.(18) Participants with greater than zero but less than 600 MET-minutes of moderate- and vigorous-intensity activity were classified as “low active”, 600 and 1,500 MET-minutes as “moderately active”, and greater than 1,500 MET-minutes as “high-active”. Participants reporting zero minutes of moderate- and vigorous-intensity activity were classified as “sedentary”. Participants were also classified as meeting or not meeting national physical activity guidelines of 150 minutes or more of weekly moderate-intensity or vigorous-intensity activity.(7)

Anthropometric and Clinical Measures—Standing height (cm) was measured using a Perspective Enterprises stadiometer (Portage, MI) and weight (kg) using a Seca digital scale (Birmingham, UK). Measures were taken twice and the mean calculated. Body mass index (BMI) was calculated as weight (kg) divided by height (m²). Blood pressure and pulse rate were measured using a random zero blood pressure machine (MK2 RandomZero – Hawksley, England) following the National High Blood Pressure Education Program protocol, where the means of the second and third measures were calculated.(19)

Biological Markers—Upon confirmation of a ten-hour fast, blood specimens were collected and fasting blood glucose was obtained using a Glucostat analyzer (Model 27, YSI, Inc., Yellow Springs, OH) at the time of specimen collection. Specimens were aliquoted and frozen at -80° C. Lipid panels, glycated hemoglobin, C-reactive protein (CRP) samples were analyzed at a CLIA-certified laboratory. Interleukin-6 (IL-6) and TNF- α , markers of chronic, low-grade inflammation were measured using multiplex ELISA (Milliplex Map, Millipore CA) and read in Luminex 200 system (Luminex Corp., Austin TX). Plasma samples were briefly spun and diluted 1:400. Following incubations and washes, beads were read in the Luminex 200 system.

Allostatic Load Scores—Following the method and high-risk criteria described by Crimmins et al. (11), biological markers were categorized into binary variables of high- or low-risk (coded as 1 or 0 respectively). The number of high-risk classifications were summed into four risk scores: (1) *blood pressure risk score* which consisted of systolic blood pressure (≥ 140 mm Hg) (20), diastolic blood pressure (≥ 90 mm Hg) and heart rate (≥ 90); (2) *metabolic risk score* comprised of total cholesterol (≥ 240 mg/dl), HDL (<40 mg/dl), BMI (≥ 30 kg/m²), and glycated hemoglobin ($\geq 6.4\%$) (11), (3) *inflammatory risk score* including CRP (>3.0 mg/L), TNF- α (>2.725 , median sample value), and IL-6 (>0.64) (21); and (4) *total allostatic load risk score*, which summed the total number of high-risk classifications. The following methods were used in calculating scores. Participants with IL-6 values below the 10th percentile were considered normal.(21) The cutoff score for TNF- α was based on the median score, as no guidance was provided in the literature. The

blood pressure, metabolic, and inflammatory risk scores were dichotomized as low (0 or 1 markers above respective cutpoints) versus high (>1 markers above respective cutpoints). Total allostatic load risk score (possible range 0-10) was dichotomized as low (≤ 3 markers) versus high (> 4 markers).

Statistical Analysis

Descriptive statistics (means and standard deviations) were calculated for age, systolic and diastolic blood pressure, pulse rate, BMI, total cholesterol, HDL, glycated hemoglobin, CRP, IL-6, and TNF- α , unadjusted minutes of physical activity by intensity level and total minutes. Median household income was calculated. Frequencies were calculated for sex, education and IPAQ classification. Education was categorized as a dichotomous variable (≥ 12 years or <12 years) due to the low frequencies in the higher education categories. Chi-square tests of association were computed for allostatic load and risk scores to assess possible differences in this sample by country of birth because differences in biological risk profiles have been reported for United States- versus Mexican-born individuals.(11)

Logistic regression models were used to assess unadjusted and adjusted associations between physical activity level with total allostatic load score and the blood pressure, metabolic, and inflammatory risk scores. A priori power calculations indicated sufficient power for examining meeting versus not meeting physical activity guidelines. Despite small group sizes in the four-category classification, logistic regression models were conducted to assess preliminary evidence of a dose-response association.(22, 23) Variables used to adjust associations included age, sex, and education. The referent for physical activity level was sedentary. Contrasts with Bonferroni post hoc adjustment were used to examine odds ratio differences among low, moderate and high active participants. Because more than one participant may have been recruited from each household, models were initially run using a nested model with household as a fixed factor. However, there were no differences between these models and the unadjusted models. Interaction terms for level of physical activity or meeting guidelines with age, sex and education were also considered in the adjusted models. All results are interpretable at $\alpha = 0.05$.

Results

Two-thirds (67.6%) of participants were born in Mexico, with the average time spent living in Cameron County being 20.57 years (± 15.33). The sample was 67.9% female, slightly more than half (57.6%) reported less than 12 years of education, and the median household income was \$14,400 annually. One-third of participants (32.4%) were born in the United States. However, there were no statistically significant differences in the allostatic load and risk categories by country of birth. Sample characteristics related to physical activity and biological risk are provided in Table 1. The level of physical activity in the sample was low: only 8.5% were moderately active and 17.0% highly active, while 8.8% were low active and 65.8% were inactive. About one-fourth (25.5%) met national guidelines for weekly physical activity. Among participants meeting recommendations, males reported more weekly minutes of vigorous or moderate-intensity activity (802.9) than females (477.6, $p=0.004$). Males reported more minutes of vigorous-intensity activity (101.2) and more total physical

activity (395.20) than females ($M_{\text{vigorous}}=34.97$; $p=.015$; $M_{\text{total}}=257.5$, $p=0.049$). Males also had lower CRP (3.90) and HDL (44.02), and higher diastolic blood pressure (74.47) than females ($M_{\text{CRP}}=5.96$, $p=.001$; $M_{\text{HDL}}=49.95$, $p<.001$; $M_{\text{diastolic}}=70.83$, $p=.001$).

Biological markers by level of physical activity are also shown in Table 1. Systolic blood pressure was significantly higher for sedentary than for moderately active participants ($p=0.005$). CRP was significantly lower in high active than in sedentary participants ($p=0.038$). No other significant differences were detected. The mean blood pressure risk score in the sample was $0.16 (\pm 0.43)$; metabolic risk score was $1.73 (\pm 0.85)$; inflammation risk score was $1.59 (\pm 0.97)$; and total risk score was $3.49 (\pm 1.57)$. There were no significant differences between foreign and US born participants.

Table 2 describes the association between meeting physical activity guidelines (yes versus no) and total allostatic load score and the three risk categories. In the unadjusted models, participants meeting physical activity guidelines were significantly less likely to be at high risk for inflammation (OR = 0.51, 95% CI: 0.31, 0.84) and total allostatic load (OR = 0.50, 95% CI: 0.31, 0.84) than participants not meeting guidelines. However, meeting guidelines was not significantly associated with any of the 4 scores after adjusting for age, sex and education.

The dose-response relation between physical activity and the allostatic load scores was also assessed by logistic regression (Table 3). There was a significant relation between high levels of activity (> 1500 MET minutes per week) and decreased risk of inflammation and total allostatic load compared to sedentary participants. These associations held after adjustment for age, sex and education ($p = 0.009$; $p = 0.015$). Additionally, contrasts analyses found that high active participants were less likely to have high allostatic load risk ($p=0.010$) and less likely to have higher inflammation scores ($p = 0.030$) compared to moderately active participants. However, there were no significant differences in risk scores across the moderate and low active groups.

Interaction effects were assessed for age, sex and education with meeting or not meeting guidelines and physical activity level. A statistically significant interaction (Figure 1) was found for meeting guidelines with sex where men meeting guidelines (OR = 0.25, 95% CI: 0.10, 0.65) and women meeting guidelines (OR = 0.75, 95% CI: 0.60, 0.94) had significantly lower inflammation risk than men not meeting guidelines (Ref). The odds ratio for women not meeting guidelines (OR = 0.74, 95% CI: 0.42, 1.32) was not significantly different than the referent group. No other significant interactions were detected.

Discussion

This study examined the association between physical activity and allostatic load in a sample of Mexican American adults living on the US-Mexico border--a population with obesity and diabetes rates greater than the national average.⁽¹⁵⁾ After adjustment for age, sex, and education, high levels of physical activity (> 1500 MET minutes weekly) were found to be associated with a lower total allostatic load score and lower inflammatory markers; moderate and low levels of physical activity were not associated with any of the

allostatic load scores. There did not appear to be a dose-response relation, as there was no trend for moderate levels of physical activity to be associated with any of the 4 allostatic load risk scores.

In addition, there was an interaction effect by sex in the association of meeting physical activity guidelines with inflammatory risk score. Men meeting guidelines had the least likelihood of high inflammatory risk scores. Women meeting guidelines also had significantly lower odds of having a high inflammatory risk score compared to men not meeting guidelines (referent group). However, the men in the study were more active than the women, so the total MET-minutes/week in the men meeting guidelines was higher than that of the women, possibly explaining the lower odds ratio for men than women meeting guidelines. Future research may explore the dose of physical activity for Mexican American men and women needed to lower inflammation.

Other studies have reported an association of physical activity with inflammatory markers, including a Greek study comparing cytokine levels in 701 active versus sedentary adults (6) and controlled exercise training trials.(24) Overall, our findings suggest that participation in physical activity at a moderate- or vigorous-intensity level may positively impact markers of chronic, low-grade inflammation. These are novel findings for this population as the association between physical activity and allostatic load in Mexican Americans has not been previously examined.

Contrary to existing evidence for non-Hispanic white adults (25), no direct associations were found between physical activity and metabolic or blood pressure risk factor scores. NHANES data suggested that Mexican American ethnicity and physical inactivity are associated with greater risk of metabolic dysregulation.(26) Possible explanations for these findings may lie in the self-reporting of physical activity and smaller sample sizes in the low and moderately active groups. Interestingly, an association was seen for inflammatory risk and total allostatic load. This may be because chronic low-grade inflammation can be a precursor to metabolic dysregulation. Using an objective measure of physical activity may improve the detection of a dose-response relationship.

The low levels of vigorous and moderate-intensity physical activity in this sample presumably made it more difficult to detect a dose response effect. There is some evidence that, unlike the average Mexican Americans in NHANES (10), Mexican-Americans on the US-Mexico border may participate in less leisure-time MVPA (27), and more light-intensity activity from occupational or household domains that are associated with low-income populations.(28) Further research is needed using objective measures of physical activity, considering leisure-time and other domains of activity, to elucidate the associations found in this study.

Interestingly, the mean scores for metabolic and inflammation risk were nearly double the risk scores reported for Mexican Americans in the NHANES 1999-2002 data analyzed by Crimmins and colleagues.(11) However, the mean blood pressure risk score in this sample was 0.16, compared to 0.45 for Mexican Americans in the Crimmins et al. sample.(11) Further, the differences by country of birth in Crimmins et al. were not present in this

sample. The prevalence of type II diabetes mellitus along the south Texas-Mexico border is nearly 30%.(15) This high rate of metabolic dysregulation may contribute to the increased metabolic risk scores in this study. Similarly, the increased inflammation risk score is cause for concern as chronic low-grade inflammation can be a precursor to development of diabetes.

These findings should be considered in the context of several limitations. The cross-sectional study design precludes any conclusions about causality of associations. The study relied on self-reported physical activity and not objective measures of physical activity. The study did not assess volume of light-intensity activity. Low-income individuals may participate in greater amounts of light-intensity activity (28) and have less time for leisure-time physical activity, the primary domain of moderate-to-vigorous intensity activity. Furthermore, self-reporting of light-intensity activity, and physical activity more broadly, is subject to recall bias particularly among Hispanics.(29, 30) Comparisons of the results with other studies are complicated by differences in the methods for calculating total allostatic load; e.g., some studies include fibrinogen and albumin in the scores, while this study did not. However, the TNF- α and IL-6 biomarkers used in this study have been included in other studies of allostatic load with non-Hispanic participants.(2) Finally, because the study power was low with small sample sizes in the Low and Moderately Active groups, a dose-response pattern may exist, but the power was not strong enough to detect it. Allostatic load represents the cumulative burden of physiologic dysregulation. Hence it should be more difficult to detect a dose-response effect in the relatively young participants of this study (mean age = 43 years), than in an older cohort.

Hispanics are the largest minority group in the United States and are two-thirds are of Mexican origin or descent.(31) There is a documented cardiovascular disease mortality disparity that favors Mexican Americans despite disproportionate rates of obesity, diabetes, and poverty.(32) Mexican Americans may have an inflammatory profile different from their non-Hispanic counterparts.(33) Similarly, inflammatory markers in recent immigrants may differ from long-term residents in the United States. Understanding the cardiovascular disease pathway among Mexican Americans is necessary for providing appropriate prevention and treatment options.

In summary, this study provides unique evidence that physical activity is associated with reduced allostatic load among Mexican-American. More research is needed on the relations between allostatic load and physical activity in Mexican American populations who have higher levels of physical activity. Research is also needed on how volume of light-intensity activity may affect allostatic load. Future studies may consider the utility of allostatic load scores that are not based only on abnormal values, but perhaps focus on variation within the normal range (e.g., high normal CRP versus low normal CRP), or a threshold for overload. Finally, research studies should examine whether effects of physical activity on allostatic load differ by sex.

Conclusion

This is the first study to describe an association between physical activity and allostatic load, and in particular chronic low-grade inflammation among Mexican American adults. Allostatic load is a framework for describing the accumulation of physiologic dysregulation. Physical activity is a modifiable risk factor for stress and most biological endpoints of allostatic load, highlighting the need for interventions that lead to a physically active lifestyle. This may be especially important among Mexican Americans who have higher rates of obesity and diabetes, and therefore may accumulate allostatic load at a faster rate, than other racial and ethnic groups in the United States.

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Figure 1.
Interaction effect of meeting physical activity guidelines by sex on likelihood of having low inflammatory risk.
Note: PA=Physical Activity

Table 1
Participant Characteristics for Age, Physical Activity and Biological Marker Variables (N=330)

Variable	Total Sample		Level of Physical Activity				p
	M	SD	Sedentary (n=217)	Low Active (n=29)	Moderately Active (n=28)	High Active (n=56)	
Age	42.82	15.33					
Physical Activity Minutes (unadjusted)							
Walking	144.21	289.32					
Moderate-Intensity	101.23	257.32					
Vigorous-Intensity	56.25	188.79					
Total	301.70	515.08					
Blood Pressure Risk Factors	0.16	0.43					
Systolic blood pressure (mm Hg)	117.21	15.80	119.35 ^a	113.93	110.54	113.98	0.005
Diastolic blood pressure (mm Hg)	72.00	9.72	72.34	73.14	70.75	70.71	0.553
Heart rate at 60s	50.91	7.97	67.44	69.10	69.71	68.07	0.658
Metabolic Risk Factors	1.73	0.85					
BMI (kg/m ²)	30.78	7.25	31.06	30.10	32.97	28.93	0.079
Total cholesterol (mg/dL)	174.78	36.08	174.29	187.55	175.82	169.55	0.182
HDL (mg/dL)	48.05	10.70	47.86	48.48	47.18	48.96	0.872
Glycated hemoglobin (HbA _{1c} %)	6.65	1.98	6.62	6.88	6.13	6.90	0.360
Inflammatory Risk Factors	1.59	0.97					
CRP (mg/L)	5.30	6.67	5.88 ^b	4.19	6.10	3.20	0.038
TNF-α (pg/ml)	3.23	4.07	3.54	2.83	2.35	2.67	0.273
IL-6 (pg/ml)	4.19	8.96	4.92	2.26	4.71	2.11	0.117
Total Allostatic Load Score	3.49	1.57	3.66	3.59	3.50	2.77	0.002

^a significant difference with Moderately Active

^b significant difference with High Active

Table 2
Logistic Regression Models Predicting High Allostatic Load and Risk Factors by Meeting Physical Activity Guidelines

	Model 1 ^a				Model 2 ^b			
	<i>b</i>	<i>SE</i>	Odds Ratio	95% CI	<i>b</i>	<i>SE</i>	Odds Ratio	95% CI
Allostatic Load	-0.69	0.26	0.50	0.30, 0.84	-0.38	0.28	0.68	0.39, 1.19
Blood Pressure Risk	-0.52	0.41	0.60	0.27, 1.33	-0.21	0.43	0.81	0.35, 1.90
Metabolic Risk	-0.24	0.25	0.79	0.48, 1.30	0.04	0.27	1.04	0.61, 1.78
Inflammation Risk	-0.68	0.26	0.51	0.31, 0.84	-0.46	0.27	0.63	0.37, 1.07

Note: (N=330). Referent is Not Meeting Guidelines.

^aModel 1 is unadjusted for covariates.

^bModel 2 adjusted for age, sex and low education (<12 years).

Table 3
Logistic Regression Models Predicting High Allostatic Load and Risk Factors by Level of Physical Activity

		Model 1 ^a				Model 2 ^b			
		<i>B</i>	<i>SE</i>	Odds Ratio	95% CI	<i>b</i>	<i>SE</i>	Odds Ratio	95% CI
<u>Allostatic Load Risk</u>									
Physical Activity Level	High	-1.13	0.33	0.32	0.17, 0.62	-0.86	0.36	0.42	0.21, 0.85
	Moderate	0.02	0.40	1.02	0.47, 2.25	0.45	0.43	1.57	0.67, 3.67
	Low	-0.19	0.40	0.83	0.38, 1.80	-0.02	0.41	0.98	0.44, 2.21
	Sedentary	--	--	1.00	--	--	--	1.00	--
<u>Blood Pressure Risk</u>									
Physical Activity Level	High	-0.60	0.51	0.55	0.20, 1.47	-0.30	0.69	0.74	0.26, 2.09
	Moderate	-0.40	0.64	0.67	0.19, 2.34	-0.00	0.66	1.00	0.27, 3.67
	Low	-0.11	0.57	0.89	0.29, 2.73	0.08	0.59	1.08	0.34, 3.45
	Sedentary	--	--	1.00	--	--	--	1.00	--
<u>Metabolic Risk</u>									
Physical Activity Level	High	-0.42	0.30	0.66	0.37, 1.19	-0.12	0.46	0.89	0.47, 1.67
	Moderate	0.24	0.42	1.28	0.56, 2.89	0.56	0.44	1.75	0.74, 4.14
	Low	0.30	0.41	1.35	0.60, 3.03	0.47	0.43	1.60	0.70, 3.69
	Sedentary	--	--	1.00	--	--	--	1.00	--
<u>Inflammation Risk</u>									
Physical Activity Level	High	-1.05	0.31	0.35	0.19, 0.65	-0.86	0.44	0.43	0.22, 0.81
	Moderate	-0.09	0.41	0.91	0.41, 2.02	0.20	0.42	1.22	0.53, 2.81
	Low	-0.31	0.40	0.73	0.34, 1.59	-0.22	0.40	0.80	0.36, 1.77
	Sedentary	--	--	1.00	--	--	--	1.00	--

Note: (N=330). Referent category is sedentary.

^aModel 1 is unadjusted for covariates.

^bModel 2 adjusted for age, sex and low education (<12 years).