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Dose–response association of physical activity with HbA1c: Intensity and bout length

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ABSTRACT

Objective. The aims of this study were to characterize the dose–response relationship between moderate-to-vigorous intensity physical activity (MVPA), and light-intensity activity with HbA1c in adults at low, moderate, and high risks of type 2 diabetes, and to compare the relationship of short (1 to 9 min) versus long (10+ min) bouts of MVPA with HbA1c.

Methods. Data from 2707 participants from the 2003–2006 National Health And Nutrition Examination Survey were analyzed in 2014–2015. Type 2 diabetes risk was classified into three groups based upon age (<40 years; ≥40 years) and BMI (<30; ≥30). The relationship between HbA1c and accelerometer-based physical activity variables was assessed using multiple regression models.

Results. There was a curvilinear dose–response relationship between HbA1c with total activity and MVPA in adults at moderate or high risk for type 2 diabetes: higher amounts of physical activity were associated with lower HbA1c. The association of physical activity on HbA1c was stronger at lower levels of physical activity. There was no dose–response relationship in adults at low risk for type 2 diabetes. The relationship between short bouts with HbA1c was stronger than for bouts ≥10 min.

Conclusions. In adults at risk for type 2 diabetes, there is a dose–response relationship between physical activity and HbA1c levels such that the relationship: (1) is curvilinear; (2) is stronger when a higher percent of total activity comes from MVPA; and (3) is more potent with short bouts of MVPA. Fractionalized physical activity of at least moderate-intensity may contribute to long-term glucose control.

Introduction

Randomized trials have provided strong evidence that physical activity (PA) improves metabolic health. In adults with impaired glucose tolerance, randomized trials show that moderate-to-vigorous intensity aerobic physical activity (MVPA) improves glucose control and reduces risk of type 2 diabetes (Hamman et al., 2006; Li et al., 2008; Pan et al., 1997). In adults with type 2 diabetes, exercise also improves glucose control. One meta-analysis reported that MVPA reduces HbA1c (glycated hemoglobin) by an average of 0.8% (Snowling and Hopkins, 2006). However, some aspects of the relationship between metabolic health and PA remain incompletely characterized.

First, there are few data on the dose–response relationship between objectively-measured (aerobic) physical activity and HbA1c. Historically, epidemiologic studies have either not measured HbA1c and/or used self-report measures of PA. The NHANES (National Health And Nutrition Examination Survey) has collected cross-sectional data on HbA1c and accelerometer-measured PA (NHANES 2003-2004, 2015a; NHANES 2005-2006, 2015b). A published study of PA and metabolic health using NHANES data reported no association of total PA or MVPA with HbA1c when considering total and bouted activity simultaneously (Wolff et al., 2014). However, healthy adults and those at risk for type 2 diabetes were not examined separately. It is difficult to infer a dose–response effect from data from randomized trials. The vast majority of trials test only one dose of activity, and the dose is typically a moderate amount of activity (in the range of 150 min of MVPA per week). For example, the meta-analysis cited above of the effect of MVPA on HbA1c included 21 studies of aerobic exercise, of which 15 studies had an average daily dose of activity between 13 and 26 min. Interestingly, the meta-analysis reported that there was not a clear dose–response effect in the randomized trial data (Snowling and Hopkins, 2006).

It also is of interest how the dose–response relationship varies by risk of type 2 diabetes. The DREW (Dose–Response to Exercise in

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postmenopausal Women) study reported only a weak dose–response effect of MVPA on fasting glucose: at the end of the trial, fasting glucose was 95.8 mg/dl in the control group versus 93.4 mg/dl in the high dose exercise group (Church et al., 2007). However, a weak dose–response effect might be expected in this trial due to a floor effect—the average fasting glucose of trial participants was in the normal range. PA presumably shows a stronger dose–response association in adults at high risk of type 2 diabetes with impaired glucose tolerance.

Second, there is incomplete information on how frequency, duration, and intensity of activity affect the dose–response relationship between PA and HbA1c. In the past, self-report has generally been used to measure frequency, duration, and intensity. Accelerometers now allow more precise measures of these features of activity. It is of interest whether relatively short (<10 min) bouts of MVPA affect HbA1c. Though current public health guidelines only recommend long bouts (10+ min) of MPVA, several studies using accelerometers report that short bouts improve metabolic health (Loprinzi and Cardinal, 2013; Luke et al., 2011). There is growing evidence that decreasing sedentary time and increasing light PA improve metabolic health (Healy et al., 2007; Loprinzi et al., 2014), though public health guidelines do not yet recommend increasing light PA (except to attain a healthy body weight). After adjusting for total volume of activity (light PA + MVPA), is MVPA relatively more effective at lowering HbA1c than light PA? Since HbA1c is aggregated continuously throughout the day, it also is plausible that spreading PA throughout the day is more effective at lowering HbA1c than infrequent, long bouts of activity.

The aims of this study were: (1) to characterize the dose–response relationship between MVPA and total PA (light, moderate, and vigorous) with HbA1c in adults at low, moderate, and high risks of type 2 diabetes, (2) to compare the effects of MVPA versus light-intensity PA on levels of HbA1c, and (3) to compare the effects of short bouts (1 to 9 min) versus long bouts (10+ min) of MVPA on levels of HbA1c.

Methods

Study population

The study used data from NHANES, which collects data in waves on a stratified, multistage probability sample of adults and youth in the United States. Participants first complete a questionnaire and then a physical examination. Nearly 14,000 individuals participated in the 2003–2004 and 2005–2006 waves of NHANES data collection. For the present study, IRB approval was not needed for the secondary analysis of de-identified, publicly available data. Participants provided informed consent to NHANES staff prior to data collection. NHANES participants were excluded from the data analyses of this study if they: (1) did not wear the accelerometer at least 4 days for 10 h per day (n = 4042); (2) were younger than 18 years (3209); (3) reported a race/ethnicity that was not Non-Hispanic White, Non-Hispanic Black, or Mexican American (n = 451); (4) were missing data on BMI or HbA1c (n = 206); or (5) had diabetes (n = 706). Participants were regarded as having diabetes if they reported a diagnosis of diabetes or were taking medication to treat diabetes (n = 638), or had an HbA1c value of 7.0% (53 mmol/mol) or greater (n = 68). An HbA1c of 7.0% or higher has high specificity and positive predictive value for undiagnosed diabetes (Li et al., 2012).

BMI and laboratory tests

NHANES participants have their height and weight measured to calculate BMI. Glycated hemoglobin was assessed using an A1c 2.2 Plus Glycohemoglobin Analyzer (Tosoh Medics, Inc., San Francisco, CA). Whole blood samples were processed in the mobile examination centers according to NHANES protocols (Glycohemoglobin in Whole Blood, 2008).

Physical activity monitors

Participants were asked to wear an ActiGraph AM-7164 (ActiGraph, Fort Walton Beach, FL) for one week. Along the lines of previous studies of NHANES data, sufficient wear time was defined as a minimum of 10 h per day on at least 4 days (Troiano et al., 2008). The NHANES accelerometer measured PA as counts/min. Standard cut points classified each minute into an intensity categories of sedentary (<100 cpm), light (100–2019 cpm), and MVPA (>2020 cpm) (Troiano et al., 2008). Total minutes, total counts, and average daily counts were calculated using data from all intensity categories. Then minutes, counts, and average counts were partitioned by intensity category (Table 1). For example, total counts = sedentary counts + light-intensity counts + MVPA counts. Values for light-intensity and MVPA counts may not add up to total counts because sedentary counts (<100 cpm) are included in the total counts variable. Daily means are used for each intensity rather than the total for each day of wear. The proportions of counts spent in MVPA and light-intensity were determined by dividing the mean daily total counts for each intensity by the daily total number of counts.

Statistical analysis

All analyses utilized the PROC SURVEY procedures in SAS version 9.3 to account for the complex sampling frame of NHANES. Descriptive statistics were calculated for sample characteristics including frequencies of race/ethnicity and gender, and means and standard errors for total accelerometer counts, MVPA accelerometer counts (≥2020) (Troiano et al., 2008), MVPA counts in short (<10 min) and long bouts (≥10 min separately), proportion of activity counts in MVPA, and in short bouts of MVPA, and light-intensity activity. The four-year sample weights were used in all analyses. Furthermore, due to oversampling of Mexican Americans in the included NHANES waves, Hispanics from countries other than Mexico, as well as other minority groups, were not included in the analyses (Analytic Note Regarding 2007–2010 Survey Design Changes and Combining Data Across other Survey Cycles, 2011).

Participants were classified as having Low, Moderate or High risk of type 2 diabetes based on age (Cowie et al., 2009) and BMI (Gregg et al., 2007). These variables were the remaining significant predictors of HbA1c in a backward selection regression model that also included HDL, triglycerides, hypertension, and parent with diabetes (Eckel et al., 2006). Participants whose age was ≥40 or BMI ≥ 30 were classified as Moderate risk. Participants with both risk factors were categorized as High risk, whereas those adults with neither risk factor were identified as Low risk. Separate one-way analyses of variance were conducted to test for differences in the accelerometer count and duration variables by diabetes risk (Table 1).

Study aims #1 and #2

The association between HbA1c and PA variables was assessed using multiple regression analysis. In all analyses, HbA1c was the dependent variable and the log values of one or more PA variables were the independent variables. Log values were used to fit the observed curvilinear relationship. The study checked the variance explained by both linear and non-linear models. The log terms for total PA and MVPA explained more variance in HbA1c (2.7%-8.9% and 3.5%-9.3% respectively) than did linear terms (1.5%-8.6% and 1.8%-9.2% respectively). Regression analyses were stratified by risk group, so that the model fit and beta coefficients could be assessed by risk. A single regression analyses with an interaction term yielded the same results.

Study aim #3

Three possible regression approaches were identified for assessing whether short bouts of MVPA have a stronger association with lower HbA1C than long bouts. The results from all three methods are reported, so as to demonstrate whether or not the findings are consistent across all three methods. The Main Effects Model adjusted for total MVPA by including log(MVPA counts); it tested whether the association between MVPA and HbA1C differed by bout length by including a term for the percent of MVPA from short bouts. The Substitution Model also adjusted for total MVPA by including log(MVPA counts); however it tested whether associations with MVPA differed by bout length using the term log(MVPA counts from short bouts) (Mekary et al., 2009). The Partition Model included log (MVPA counts from short bouts) and log (MVPA counts from long bouts) (Mekary et al., 2009). With a hypothesis that *more* short bout MVPA is associated with *lower* HbA1c, the beta coefficients for the short bout terms in the models should be negative.

Results

Table 1 shows characteristics of the NHANES participants included in the analysis according to risk group. Participants in the Low Risk group accumulated significantly more total counts (P = 0.0001) and MVPA