Physical Activity May Facilitate Diabetes Prevention in Adolescents

Amy S. Thomas, MPH\textsuperscript{a}; Lori F. Greene, MS\textsuperscript{a}; Jamy D. Ard, MD\textsuperscript{a}; Robert A. Oster, PhD\textsuperscript{b}; Betty E. Darnell, MS\textsuperscript{c}; Barbara A. Gower\textsuperscript{a}, PhD.

\textsuperscript{a}Department of Nutrition Science; \textsuperscript{b}Department of Medicine; \textsuperscript{c}General Clinical Research Center, University of Alabama at Birmingham, Birmingham, AL 35294

Corresponding Author:
Amy S. Thomas, MPH, RD
amysusan@uab.edu

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Objective: The aim of this study was to examine the association of PA with glucose tolerance and resting energy expenditure (REE) among adolescents.

Research design and methods: Subjects were 32 male and female adolescents aged 12-18 yr. Intravenous glucose tolerance (KG) and REE were assessed under inpatient conditions after an overnight fast. KG was determined as the inverse slope of time vs (ln) glucose over minutes 8-19 of an intravenous glucose tolerance test. PA was assessed over 8 d using accelerometry (counts/min).

Results: In multiple linear regression analysis, KG was positively associated with total PA, moderate PA, and moderate 5-min bouts of PA. Similarly, REE was positively associated with TPA, moderate PA, and 5-min bouts of moderate PA.

Conclusion: In this population, PA was positively related to both glucose tolerance and resting energy expenditure. These results suggest that moderate activity may be beneficial in the prevention of diabetes in adolescent populations both through promoting efficient glucose disposal and through increasing energy expenditure.
Traditionally, type 2 diabetes has been considered a disease primarily affecting adults; however, in the last decade, there has been an increasing and alarming incidence of type 2 diabetes in adolescent populations. While type 1 diabetes remains the prevailing form in teens in the United States, the prevalence of type 2 is expected to be predominant in many ethnic groups within 10 years (1). The first large scale, population-based study of diabetes in American youth, SEARCH, found that in 2001, 3.5% of the 10-19 year old study population had type 2 diabetes (2). Furthermore, the American Diabetes Association states that one in six overweight adolescents has pre-diabetes (3). The epidemic is imminent; escalating rates of diabetes are paralleling that of the epidemic of childhood obesity (4).

There is, however, convincing evidence in adults that increased physical activity (PA) can prevent or delay the development of type 2 diabetes. Large adult prevention trials such as the Diabetes Prevention Program (DPP) (5) and the Finnish Diabetes Prevention Group (6) showed intensive lifestyle interventions, including exercise, to be 58% more effective in retarding progression from impaired glucose tolerance (IGT) to diabetes than the control. Remarkably, lifestyle intervention in the DPP study also resulted in 39% less incidence of diabetes than pharmacological intervention (metformin) (5). The Da Qing IGT and Diabetes Study (7) showed exercise alone reduced risk of disease progression by 46%. There have been no trials in pediatric populations to evaluate progression of IGT to diabetes. Whether the results of prevention trials in adults can be extrapolated to adolescents is unclear.

Randomized, controlled clinical trials reiterate the conclusions drawn from prevention trials with physiological evidence. Exercise has been shown to enhance insulin signaling and consequently, increase the rate of insulin-stimulated glucose uptake by GLUT 4 glucose transporter proteins (8). Independent of insulin signaling, muscle contraction also results in increased abundance and redistribution of GLUT 4 (9), the promotion of muscle mass, capillary recruitment (10), and capillary proliferation (11) in muscles, and a higher proportion of insulin-sensitive muscle fiber types (12) thereby increasing overall insulin sensitivity (13). Current research suggests that exercise promotes partitioning of excessive fatty acid uptake within the muscle to triglycerides as opposed to fatty acid intermediates known to ultimately induce insulin resistance (8).

In addition to acute promotion of glucose uptake, chronic exercise may decrease risk for type 2 diabetes via increasing energy expenditure, and thereby, limiting gains in fat mass. Exercise can increase energy expenditure directly related to the exercise bout, leisure time energy expenditure (14), and resting energy expenditure (REE). The increase in REE can occur both due to an increase in skeletal muscle mass (15) and, with vigorous exercise, excess post-exercise oxygen consumption for 24-48 hours (16).

The purpose of this study was to examine the association of PA, as assessed by accelerometry, with both glucose tolerance and REE in an adolescent population. Specifically, we hypothesized that time and intensity of physical activity would be positively associated with both glucose tolerance ($K_g$) and REE.

**RESEARCH DESIGN AND METHODS**

**Subjects**—This study was part of the longitudinal parent study, “Intra-abdominal fat and risk of disease in adolescents,” conducted at the University of Alabama at Birmingham. Subjects were recruited through
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Informational fliers, notices posted in pediatric office waiting rooms, and newspaper advertisements. The parent study excluded adolescents taking medications known to affect body composition or physical activity (ex. Prednisone, Ritalin, growth hormone) and diagnoses of syndromes known to affect body composition/fat distribution (ex. Cushing’s Syndrome, Downs’ Syndrome, type 1 and 2 diabetes, hypothyroidism). Children with any confounding medical conditions, acute or chronic, were also excluded from participation. All current subjects of the parent study were given the opportunity to participate in this sub-study.

Participants in the sub-study were 32 African American and Caucasian adolescents between the ages of 12 and 18 years, 56% female, and 47% African American (AA). Further, there were ten Caucasian male, eight Caucasian female, four AA male, and ten AA female subjects. This study was approved by the Institutional Review Board for Human Use at the University of Alabama at Birmingham. Each subject signed an assent form, and the guardian signed a consent form prior to enrollment.

**Protocol**—All data were collected during one inpatient visit to the General Clinical Research Center (GCRC) at UAB Hospital and Clinics and one follow-up visit eight days later. On the afternoon of admission to the GCRC, body composition was assessed using dual energy x-ray absorptiometry (DXA) in the Energy Metabolism Laboratory at the UAB Department of Nutrition Sciences. The morning after admission consisted of measurement of REE by indirect calorimetry and $K_g$ by intravenous glucose tolerance test. At midday, teens were fitted with accelerometers and discharged. At the follow-up visit, accelerometers were turned in to investigators for data analysis.

**Accelerometry**—Free living PA was assessed with Computer Science and Applications ActiGraph (CSA) monitors (model 7164, version 2.2, MTI Health Services, Fort Walton Beach, FL). The monitor is a small, lightweight, unidirectional accelerometer that measures vertical acceleration and deceleration. “Counts” are the summation of the accelerations measured in one minute, and acceleration is measured 10 times each second. Therefore, 600 measurements are summed and recorded at the end of one minute.

Parent and teen were given verbal and written instructions for wearing the CSA ActiGraph, and an investigator secured the monitor above the iliac crest of the right hip with an elastic band prior to discharge from the GCRC. The monitor was programmed to begin collecting data at 12:00 pm on the day of discharge. The subject wore the activity monitor 24 hours a day for 8.5 days, except when swimming and bathing. The first 12 hours of data were not analyzed but regarded as a period of adaptation. The outcome variables were total body movement (counts/day), which is an indicator of the total volume of physical activity, and time (minutes/day) spent at different activity intensity categories. At the end of the collection period, counts were categorized to the following groups:

- `<1952 counts = < 2.99 METS (walking >24 min/mile) = light activity`
- `1953-5724 counts = 3.0-5.99 METS (walking 15-24 min/mile) = moderate activity`
- `5725-9498 counts = 6.0-8.99 METS (jogging 8-15 min/mile) = hard activity`
- `>9499 counts = > 9.0 METS (running <8 min/mile) = very hard activity (17).`

Mean number of 5-, 10-, and 20-minute bouts per day of moderate physical activity were also calculated.

**Body Composition**—Total fat mass and fat free mass were determined via DXA using a Lunar Prodigy densitometer (GE-Lunar Corp, Madison, WI, with software version 6.10.029). Subjects were scanned in
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the supine position with their hands placed at their sides. For the purposes of this paper, we will refer to measures of fat free soft tissue as fat free mass (FFM). At the GCRC, height and weight were recorded to the nearest 0.1 centimeter and kilogram, respectively. A standardized stadiometer and a Scale-tronix digital scale were used for measurements.

Resting Energy Expenditure (REE)—Each adolescent fasted for at least eight hours following an evening admission. Each participant’s resting metabolic rate was measured using a Delta Trac 2 Metabolic Cart (Sensor Medics, Anaheim, CA, USA) in the morning immediately upon awakening. After calibration using standard gases, the clear plastic canopy was placed over the subject’s head. Following a 5-minute acclimation period, respiratory gas exchange was measured for 25 minutes, and the average REE calculated.

An in-house, quality control, alcohol burn test was performed quarterly on the Delta Trac instrument, or whenever questions or problems arose. At all times during the project period, the instrument generated respiratory quotient values between 0.64 and 0.69, which are reflective of accurate function, as indicated in the manufacturer’s guidelines. In addition, the instrument was serviced annually by the manufacturer to assure accurate function and calibration.

Intravenous Glucose Tolerance Test—At approximately 7:00 am, after a 12-hour fast, flexible intravenous catheters were placed in the antecubital spaces of both arms. At time “zero,” glucose (300 mg/kg) was administered intravenously. At minute 20 following glucose administration, subjects received a 5-minute infusion of insulin (0.02 units/kg). Blood samples were collected at -30, -15, 1, 2, 3, 4, 5, 6, 8, 10, 12, 15, 19, 20, 21, 22, 24, 25, 26, 28, 30, 35, 40, 50, 60, 70, and 240 minutes relative to glucose injection. Sera subsequently were analyzed for glucose and insulin, and values were entered into the MINMOD computer program (version 3.0, © Richard N. Bergman) for determination of the insulin sensitivity index (SI) and the acute insulin response to glucose (AIRg). AIRg is the integrated incremental area under the curve for insulin during the first 10 minutes of the test. The average of the -30 and -15 min glucose and insulin values were used for determination of basal glucose and insulin concentrations. Intravenous glucose tolerance (Kg, %/min) was determined from the inverse slope of the regression line of time (min) vs. ln glucose (mg/dL) from minute 8 through minute 19 of the test. A higher number implies higher (“better”) glucose tolerance. Intravenous glucose tolerance is the rate at which glucose declines following administration, which primarily reflects glucose uptake and utilization by skeletal muscle. Glucose tolerance was assessed because it captures several processes that affect glucose disposal, including insulin sensitivity, beta cell responsiveness, hepatic insulin extraction, insulin suppression of glucose production, vascularization of skeletal muscle, and skeletal muscle perfusion. All of these processes may be affected by aspects of physiology, metabolism, and the environment. Thus, glucose tolerance is an integrated measure of numerous processes that affect the ability to dispose of glucose.

Assay of Glucose and Insulin—Analyses were performed in the Core Laboratory of the GCRC and the Clinical Nutrition Research Center at UAB. Glucose was measured in 10 µl sera using an Ektachem DT II System (Johnson and Johnson Clinical Diagnostics). Insulin was assayed in duplicate 100 µl aliquots with Linco Research Products Inc. (St. Charles, MO) reagents. In the Core Laboratory, this assay has a sensitivity of 3.35 µIU/ml, a mean intra-assay c.v. of 3.49%, and a mean interassay c.v. of 5.57%. Commercial quality control sera of low, medium, and high insulin
concentration are included in every assay to monitor variation over time.

**Statistical Methods**—Descriptive statistics were computed for the PA variables, REE, metabolic variables, and demographic variables. \( K_g \) and \( S_i \) values were log transformed (using a log10 scale) to follow an approximate normal distribution. Differences between ethnic groups and gender were examined (separately) using two-group t-tests, or the two-group t-test for unequal variances as appropriate. Relationships between PA variables and \( K_g \) were examined using Pearson correlation analysis. Multiple linear regression models were developed for predicting \( K_g \) and REE. For the \( K_g \) model, the independent variables were total physical activity (TPA), very hard physical activity (VHPA), hard physical activity (HPA), moderate physical activity (MPA), and moderate 5-min bouts of PA, each used in a separate model; covariates in all models were race, gender and total fat mass. Though race and fat mass are not significant in the model, both are known determinants of glucose metabolism and therefore \( K_g \). We elected *a priori* to include both. For the REE model, independent variables were TPA, VHPA, HPA, MPA, and moderate 5-min bouts of PA, each used in a separate model; covariates used in all models were race and FFM. In preliminary regression models, gender was examined as a predictor of REE, and was found not to be statistically significant \((P>0.05)\); thus, gender was not included in the final model. All statistical tests used a significance level of 5% and were two-tailed. Statistical analyses were performed using SAS, version 9.1 (SAS Institute Inc., Cary, NC, USA).

**RESULTS**

Study population demographics are described in Table 1. Female subjects had significantly higher fat mass \((p=0.0124)\), higher % fat \((p=0.0002)\), lower FFM \((p=0.0001)\), lower REE \((p=0.0173)\) and higher \( K_g \) \((p=0.0171)\) than male subjects. There were no significant differences in demographic or metabolic characteristics between groups of AA and Caucasian subjects.

Male subjects engaged in significantly more TPA, MPA and HPA \((p=0.0108, p=0.0379, p=0.0329, \text{ respectively})\) than female subjects (Table 2). Race was a determinant of total activity counts (TAC) and was significantly higher in AA teens than Caucasian. Race was not a determinant of minutes spent in TPA, MPA, HPA or VHPA.

Multiple linear regression analysis indicated significant, independent associations between \( K_g \) and TPA \((p=0.026; \text{Figure 1})\), MPA \((p=0.031)\), and 5-minute bouts of MPA \((p=0.035)\). HPA and VHPA did not make significant contributions to \( K_g \) \((p=0.717, p=0.830, \text{ respectively}; \text{data not shown})\).

A positive, independent relationship was observed between REE and TPA \((p=0.016; \text{Figure 2})\), MPA \((p=0.032)\), HPA \((p=0.040)\), and 5-minute bouts of MPA \((p=0.011)\). VHPA was not independently associated with REE \((p=0.507; \text{data not shown})\).

**CONCLUSIONS**

The aim of this study was to examine the association of PA with \( K_g \) and REE in an adolescent sample. In this study, PA was positively associated with both \( K_g \) and REE. The relationship between PA and carbohydrate metabolism is well-established in adult populations; however, this research provides new information in teen-aged populations, and may be important as obesity-related diseases, such as diabetes, expand into this age group. Further research is needed to determine if moderate physical activity can decrease risk for obesity and glucose intolerance in this population.
The significant differences in percent body fat, FFM, and REE between males and females in this study verify findings of previous research in an adolescent population (18). We did not see REE differences between ethnicities in this study. Similarly, our previous research in young children indicated that REE was similar in AA and Caucasian (19). Other literature showed that Caucasian teens as a group had higher REE than AA teens, but when analyzed for sex, Caucasian boys had lower REE than AA boys, whereas the opposite was true for girls (18). It is possible that the reported ethnic difference in REE is sex-specific, and that it develops during adolescence.

Assessment of K_g in an adolescent population is a novel undertaking. In this study, K_g was higher in girls than boys, independent of body composition, race, and physical activity. Sex differences in aspects of glucose metabolism have been attributed to an estrogenic hormonal environment. Estrogen stimulates skeletal muscle glucose uptake (20), which is reported to be greater in women than men (21). This study suggests that sex differences in glucose metabolism are apparent in adolescence.

The study sample engaged in approximately 40 minutes of PA per day, the majority spent in a moderate level of PA. Less than 5 minutes per day were spent in HPA and less than 1 minute per day in VHPA. This cohort engaged in few bouts of vigorous PA (22). In our study sample, males engaged in significantly more PA than females, also consistent with other literature (23). When comparing the TPA of Caucasians and AA, there were no statistically significant differences. Other literature also suggests greater similarities in PA among ethnic groups than gender groups, although AA adolescent populations were less active than Caucasian (24).

We saw a significant association between K_g and TPA (Figure 1), MPA, and 5-minute bouts of MPA. Exercise is a major mediator of glucose transport activity in muscle, and this occurs through an increase in the maximal velocity of transport (13). Another major mechanism that increases glucose uptake through exercise is by the translocation of glucose transporter proteins from an intracellular compartment to the surface of the cell. Because exercise affects glucose transport through several mechanisms, we do not know the exact mechanism responsible for the relationship observed in this study between PA and K_g. The absence of relationships in this study of K_g with HPA and VHPA may have been due to the minimal amounts of these activities performed by this study sample.

Our results indicate that, as total (Figure 2), moderate, and hard physical activity increased, an adolescent’s mass-specific REE increased. Data from adults also indicate that exercise can increase REE, adjusted for FFM (16). Our observation of a positive association between PA and REE suggests that promotion of movement, such as leisure-time activity and planned exercise, among adolescents may be a particularly useful means of combating obesity within this age group. However, further research is needed to determine if an intervention to increase PA will likewise increase REE.

Strengths of the study include robust measures of K_g and time spent in moderate to vigorous PA. Limitations include a relatively small sample size (n=32) which may have limited our ability to detect racial differences among outcomes of interest. In particular, the small number of AA males may have constrained the outcomes further. A limitation of this and all cross-sectional studies is that causality cannot be inferred from statistical relationships. Further
research is needed to determine if a physical activity intervention is associated with changes in REE and $K_g$. Additionally, the ActiGraph may underestimate sedentary and light intensity PA.

In conclusion, adolescents in this study engaged primarily in MPA, with very little HPA or VHPA. PA was significantly associated with $K_g$ and REE. Longitudinal studies with a larger population are needed to determine whether an increase in physical activity results in increases in REE and $K_g$, and if so, to examine the relevant mechanisms involved. Likewise, further research is needed to determine if consistent PA increases REE and limits obesity in the adolescent population.

ACKNOWLEDGEMENTS

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REFERENCES
**Table 1.** Baseline demographic and metabolic characteristics (mean +/- SD); all subjects combined and by ethnic and gender groups.

<table>
<thead>
<tr>
<th></th>
<th>Total Population (n=32)</th>
<th>Caucasian (n=18)</th>
<th>African American (n=14)</th>
<th>Male (n=14)</th>
<th>Female (n=18)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>16.0 +/- 1.6</td>
<td>16.1 +/- 1.3</td>
<td>15.9 +/- 2.0</td>
<td>15.9 +/- 1.5</td>
<td>16.1 +/- 1.8</td>
</tr>
<tr>
<td>Tanner Stage</td>
<td>4.8 +/- 0.5</td>
<td>4.8 +/- 0.5</td>
<td>4.9 +/- 0.3</td>
<td>4.9 +/- 0.4</td>
<td>4.8 +/- 0.5</td>
</tr>
<tr>
<td>Weight-for-Height Percentile</td>
<td>66.2 +/- 32.1</td>
<td>57.4 +/- 37.1</td>
<td>77.3 +/- 20.4</td>
<td>60.1 +/- 31.0</td>
<td>70.8 +/- 33.0</td>
</tr>
<tr>
<td>Total Fat Mass (kg)</td>
<td>23.4 +/- 15.5</td>
<td>22.2 +/- 15.8</td>
<td>24.9 +/- 15.6</td>
<td>15.8 +/- 15.0</td>
<td>29.3 +/- 13.5*</td>
</tr>
<tr>
<td>% Fat</td>
<td>29.5 +/- 14.2</td>
<td>30.0 +/- 13.7</td>
<td>28.9 +/- 15.4</td>
<td>19.7 +/- 12.4</td>
<td>37.5 +/- 10.1*</td>
</tr>
<tr>
<td>Total FFM (kg)</td>
<td>45.7 +/- 12.1</td>
<td>45.6 +/- 10.5</td>
<td>45.8 +/- 14.3</td>
<td>54.1 +/- 8.7</td>
<td>39.2 +/- 10.3*</td>
</tr>
<tr>
<td>REE (kcal/d)</td>
<td>1565 +/- 253</td>
<td>1602 +/- 309</td>
<td>1524 +/- 171</td>
<td>1688 +/- 283</td>
<td>1471 +/- 185*</td>
</tr>
<tr>
<td>$S_i$ ($x10^4$min$^{-1}$/µIU/ml)</td>
<td>3.41 +/- 1.87</td>
<td>3.46 +/- 2.15</td>
<td>3.36 +/- 1.49</td>
<td>3.77 +/- 2.12</td>
<td>3.12 +/- 1.65</td>
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<tr>
<td>$K_g$ (%/min)</td>
<td>2.15 +/- 1.21</td>
<td>1.83 +/- 0.87</td>
<td>2.57 +/- 1.47</td>
<td>1.63 +/- 0.67</td>
<td>2.56 +/- 1.38*</td>
</tr>
</tbody>
</table>

*Significantly different between male and female subjects (p<0.05)

**Table 2.** Mean physical activity by accelerometry (+/- SD); all subjects combined and by ethnic and gender groups.

<table>
<thead>
<tr>
<th></th>
<th>Total Population (n=32)</th>
<th>Caucasian (n=18)</th>
<th>African American (n=14)</th>
<th>Male (n=14)</th>
<th>Female (n=18)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TAC (counts/d)</td>
<td>382,863 +/- 144,581</td>
<td>325,962 +/- 133,681</td>
<td>456,021 +/- 127,402*</td>
<td>426,980 +/- 146,056</td>
<td>348,550 +/- 137,681</td>
</tr>
<tr>
<td>TPA (min/d)</td>
<td>41.5 +/- 27.8</td>
<td>34.8 +/- 27.8</td>
<td>50.2 +/- 26.2</td>
<td>55.3 +/- 28.7</td>
<td>30.8 +/- 22.3†</td>
</tr>
<tr>
<td>MPA (min/d)</td>
<td>37.7 +/- 24.7</td>
<td>30.8 +/- 24.7</td>
<td>46.6 +/- 22.8</td>
<td>47.9 +/- 26.2</td>
<td>29.8 +/- 21.1†</td>
</tr>
<tr>
<td>HPA (min/d)</td>
<td>3.0 +/- 5.8</td>
<td>3.3 +/- 7.5</td>
<td>2.8 +/- 3.0</td>
<td>6.0 +/- 8.0</td>
<td>0.8 +/- 1.2†</td>
</tr>
<tr>
<td>VPA (min/d)</td>
<td>0.4 +/- 1.2</td>
<td>0.3 +/- 0.4</td>
<td>0.8 +/- 1.9</td>
<td>0.9 +/- 1.8</td>
<td>0.2 +/- 0.4</td>
</tr>
</tbody>
</table>

*Significantly different between AA and Caucasian subjects (p<0.001)
† Significantly different between male and female subjects (p<0.05)
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Figure 1. Glucose tolerance relative to total daily minutes spent in physical activity after adjusting for fat mass, gender and race. (Significant at p=0.026.) Abbreviations: Kg=glucose tolerance; TPA=total physical activity

Figure 2. Relationship between REE and TPA after adjusting for race and FFM. (Significant at p=0.016.) Abbreviations: REE=resting energy expenditure; TPA=total physical activity; FFM=fat free mass