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Effects Of Exercise On Insulin Resistance In South Asians And Europeans

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ABSTRACT

G.J.G. Davey, J.D. Roberts, S. Patel, T. Pierpoint, I.F. Godsland, B. Davies and P.M. McKeigue. **Effects Of Exercise On Insulin Resistance In South Asians And Europeans**. **JEP**online, 3(2):6-11, 2000. Insulin resistance underlies coronary heart disease and type II diabetes in South Asians and Europeans. We investigated whether exercise training could ameliorate insulin resistance, and whether any benefit depended on the timing of measurement in relation to exercise. Ninety-two sedentary South Asian and European men and women aged 35-49 years were recruited. After baseline measurements, subjects were randomized to one of three groups: no change in daily activity (NE), exercise with follow up insulin sensitivity measured within 24 hours of last exercise session (E1), and exercise with follow up insulin sensitivity measured five days after last session (E5). Insulin sensitivity was determined by minimal model analysis of glucose and insulin concentrations. Maximal oxygen uptake was measured using a graded exercise treadmill test based on a modified Bruce protocol. Data from E1 and E5 showed a significant increase in cardiorespiratory fitness compared to NE (+4.15 vs. -0.003 mL/kg/min, $p<0.001$). Insulin sensitivity was significantly improved only in E1 compared to NE or E5 (+0.67 vs. +0.30 min/pmol/L, $p=0.05$), representing a 40% mean increase on initial values. In conclusion, exercise improved insulin sensitivity by 40% among those in whom it was measured within 24 hours of the final exercise session. An effect of this magnitude has considerable implications for the prevention of non-insulin-dependent diabetes at the population level.

Key Words: exercise; insulin resistance; maximal oxygen uptake; ethnic; intravenous glucose tolerance test

INTRODUCTION

The cluster of metabolic disturbances termed the insulin resistance syndrome was first described in association with non-insulin-dependent diabetes mellitus (NIDDM) and coronary heart disease in Europeans and Native Americans (1). Hyperinsulinemia, hypertriglyceridemia, hypertension, low HDL-cholesterol, and a tendency to accumulate intra-abdominal fat were later found to be prominent in people originating from India, Pakistan and Bangladesh ("South Asians") (2,3). These abnormalities are apparent from a young age (4), and together with type II

diabetes underlie the high risk of coronary heart disease in this population (5,6).

Interventions to diminish insulin resistance and hence the risk of NIDDM and coronary heart disease (CHD) are urgently needed. Several interventions have been proposed, including weight loss (7), exercise (8,9), thiazolidinediones (10) and omega-3 fatty acids (11). We tested the effect of an exercise programme among South Asians and Europeans with features of insulin resistance, but with normal glucose tolerance according to World Health Organization standard classification.

METHODS

The study was a randomized controlled trial. The duration of intervention was 12 weeks, and five successive but overlapping cohorts were formed to eliminate seasonal variation, thus the intervention part of the study ran from May 1995 to April 1996.

Ethical Approval

The study design and informed consent was approved by committees at the London School of Hygiene and Tropical Medicine, the Wynn Department of Metabolic Medicine, and Ealing, Hammersmith and Hounslow Health Agency.

Sample Size

A sample size of 15 subjects in each group was calculated to have 90% power to detect at 5% significance a change in insulin sensitivity of 36% (assuming 3-month within-subject coefficient of variation for insulin sensitivity of 30% - unpublished data). We recruited 90 participants to allow for potential dropouts.

Recruitment

Participants were recruited in a three-stage process. Lists of people registered with ten family practices in West London were used for an initial mailshot. Those responding to the mailshot were invited to attend an examination at a nearby health center. Self-reported ethnicity was established at this visit. Those with hyperlipidemia, abnormal glucose tolerance, ischemic changes on resting ECG, body mass index >40kg/m^2 and intolerance of venepuncture were excluded. Sedentary people in the highest third of an index for insulin resistance (based on fasting insulin, glucose and triglycerides, waist hip ratio and family history of type II diabetes) were invited to participate. Those who agreed to participate performed a familiarization session on an exercise treadmill, which included the completion of the first three stages of the Bruce protocol (12).

Baseline measures

The same procedures were performed on participants before randomization, in order to minimize post-randomization dropout. The procedures consisted of an intravenous glucose tolerance test (IVGTT) and an exercise test for determination of maximal oxygen uptake (VO_2max).

The IVGTT was performed using a high dose of glucose (0.5g/kg), no tolbutamide, and a reduced sampling schedule. Participants prepared for this by consuming a carbohydrate-rich (at least 200g/day) diet in the 3 days leading up to the test, and fasting from 9pm the night before. Fasting samples were taken for glucose, insulin and lipids, and a 50% D-glucose was then given via an antecubital vein over 3 minutes, and blood samples were collected at 3, 5, 7, 10, 15, 20, 30, 45, 60, 75, 90, 120, 150, and 180 minutes. Height and weight were measured, and a questionnaire on tobacco and alcohol consumption, diet, family history and daily activity was administered.

Insulin sensitivity (S_i) was measured using Bergman's minimal model of glucose disappearance (13), using programs written in Fortran 77 run on a PDP-11/83 microcomputer. The relatively high glucose dose (0.5 g/kg rather than 0.3 g/kg) employed provides for a sufficient endogenous insulin response in non-diabetic volunteers without recourse to additional augmentation of pancreatic insulin secretion. This

is apparent in the high rate of model identification (96%) and good correlation with measures of insulin sensitivity derived from the euglycaemic clamp (r=0.92) that we have found at the higher glucose dose (14,15).

The test of VO_2max was completed using a symptom limited graded exercise treadmill test (GXT) with a modified Bruce protocol (12). Speed and elevation were increased incrementally every 3 minutes. Breath-by-breath analyses of oxygen, carbon dioxide and ventilation were recorded using an on-line computerized gas analysis system (Mjinhardt Oxycon Champion System, Jaeger, UK). Heart rate, blood pressure, rating of perceived exertion and blood lactate were measured every 3 minutes, the latter being measured using a YSI Lactate Analyzer (Yellow Springs, OH). VO_2max was established when at least two of the following conditions were met: (a) a plateau or decrease in oxygen uptake associated with an increase in workload, or (b) a respiratory exchange ratio (RER) >1.15.

Randomization

Ninety-two participants were coded, the codes entered into a computer randomization routine and randomized to three groups stratified by sex and ethnicity. These groups were, no change in physical activity/wait list (NE), exercise intervention with follow up tests 24 hours after last session (E1) and exercise intervention with follow up tests 5 days after last session (E5).

Exercise Intervention

Participants randomized to exercise were given individually tailored exercise programs, requiring them to perform three half-hour sessions of interval walk/jogging (or later jog/running) to 65-75% of VO_2max assessed by heart rate extrapolated from the exercise test, plus one supervised aerobic circuit session per week. Compliance was monitored by weekly diary records and waistband actometers.

Follow-up measures

IVGTT and GXT were repeated at the end of the intervention, with the timing of the follow-up IVGTT being related to a participant's final exercise session as determined by randomization group for exercisers (E1 or E5). Anthropometry was repeated at the IVGTT appointment, and questionnaire-led checks were made on changes in general health, diet and activity during the intervention period. Five people dropped out during the intervention, so follow-up measures were performed on 87 participants.

Data analysis

Data was analysed using Stata4.0 for Windows. Natural log or square root transformations were performed on any quantitative variables whose distribution was skewed. Chi-squared tests were performed for differences in proportions of binary variables. T-tests were used to compare means of quantitative variables whose standard deviations were equal, and Wilcoxon's Rank Sum test for those whose standard deviation were significantly different. One-way analysis of variance was employed to compare means across more than two groups where the standard deviations were equal, and the F-test was used to evaluate the significance of these comparisons. Data are presented as mean±SD.

Table 1. Mean±SD baseline variables by sex and ethnic group.

Variable	Men		Women	
	European	South Asian	European	South Asian
Height (cm)	175.5±4.8	171.6±6.9	164.9±4.9	159.5±4.9
Weight (kg)	79.1±6.8	74.5±8.0	65.4±7.8	65.6±7.2
Systolic BP (mmHg)	115.3±12.4	114.0±12.4	108.5±10.4	107.5±12.9
Diastolic BP (mmHg)	73.0±8.3	76.8±10.4	68.1±11.6	68.4±8.2
BMI (kg/m^2)	25.7±2.0	25.2±2.1	24.1±2.5	25.8±2.7
WHR	0.92±0.04	0.94±0.04	0.80±0.05	0.84±0.05
Si (min/pmol/L)	2.182±0.29	1.626±0.23	2.901±0.38	1.325±0.12
VO_2max (ml/kgmin)	39.4±4.2	35.4±4.1	30.7±4.7	24.3±4.0

S_i = insulin sensitivity

Table 2. Mean±SD baseline variables by exercise group.

Variable	NE	E1	E5
Male:female	19:11	19:11	17:10
Age (years)	41.6±3.8	42.4±3.9	41.9±4.4
European:South Asian	15:15	16:14	16:11
Proportion current smokers	0.13	0.1	0.22
Proportion family history DM	0.1	0.3	0.3
BMI (kg/m^2)	25.4±2.7	25.4±2.3	24.8±1.9
WHR	0.89±0.01	0.89±0.01	0.89±0.01
Si (min/pmol/L)	2.09±0.28	1.66±0.32	2.36±16.1
VO_2max (ml/kg/min)	33.6±07.1	34.4±6.6	34.1±6.1

S_i = insulin sensitivity

RESULTS

87 participants completed the intervention. Data for baseline variables, grouped by gender, are shown for each of the groups in Table 1.

Baseline characteristics of participants did not differ significantly between randomization groups, and are shown in Table 2. However, mean waist-hip ratio was lower among Europeans than South Asians within each sex (0.92 vs 0.94, p=0.036 for men; 0.80 vs 0.84, p=0.026 for women). Maximal oxygen uptake (VO_2max) at baseline was significantly higher among men than women. VO_2max was higher among Europeans than South Asians (35.7±6.2 vs. 32.0±6.5 mL/kg/min, p=0.009), with significance persisting after adjustment for sex and age.

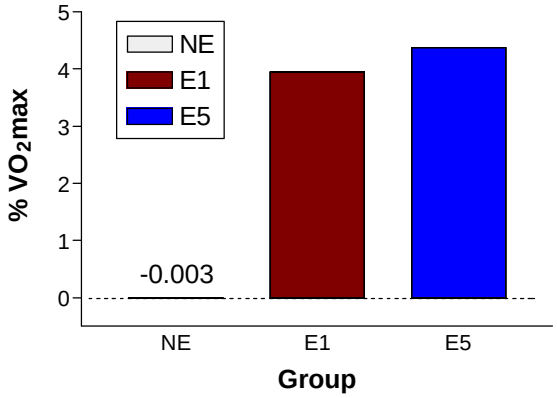

Figure 1. Changes in VO_2max by group.

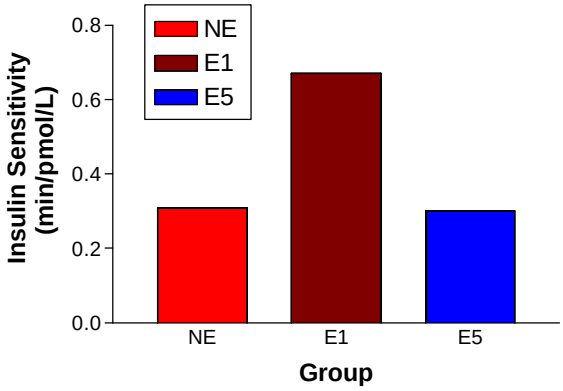

Figure 2. Changes in insulin sensitivity by exercise group.

Table 3 shows changes in variables during the intervention, by randomization group. Fitness increased significantly in E1and E5 compared to NE (+4.15 vs.-0.003 mL/kg/min, p<0.0001), representing a mean change of 12.1% on baseline levels (Figure 1). This persisted after controlling for age, sex, ethnicity and baseline BMI. There were no significant between-group differences in fitness change comparing E1 and E5.

Insulin sensitivity was found to increase significantly in E1 compared to NE and E5 (0.67 vs. 0.31 and 0.30 min/pmol/L, p=0.05, Figure 2), the significance increasing (to p=0.031) after adjustment for age, sex, ethnicity and baseline BMI. The increase in E1 represented a mean increase of 40%.

DISCUSSION

Before addressing the substantial problems represented by population-based interventions, it is important first to establish whether a proposed intervention is worthwhile in principle and likely to be effective. This study has demonstrated that a sizeable and significant increase in insulin sensitivity is achievable with exercise in a group of motivated South Asians and Europeans.

The 12% increase in VO_2max with twelve weeks of supervised exercise is consistent with other interventions of similar duration (9,16,17). Mean insulin sensitivity increased by 40% among those randomised to exercise whose IVGTTs were performed within 24 hours of the final session.

Table 3. Mean (95% CI) changes in variables during trial by exercise group.

Variable	NE	E1	E5
Weight (kg)	0.34 (-0.23 to 0.91)	0.14 (-0.47 to 0.75)	-0.03 (-0.63 to 0.57)
BMI (kg/m^2)	0.09 (-0.10 to 0.28)	0.07 (-0.13 to 0.23)	-0.03 (-0.24 to 0.19)
WHR (x10^2)	-0.6 (-1.2 to -0.1)	-1.3 (-2.0 to –0.7)	-1.5 (-2.2 to –0.9)
VO_2max (ml/kg/min)	0.00 (-0.82 to 0.81)[a]	3.95 (2.94 to 4.97)[a]	4.36 (3.13 to 5.61)[a]
Si (min/pmol/L)	0.31 (-0.35 to 0.98)[2]	0.67 (0.06 to 1.27)[b]	0.30 (-0.27 to 0.87)[b]

Key: [a]E1 and E5>NE, p<0.001; [b] E1>NE and E5, p=0.05. S_i = insulin sensitivity

This is comparable to other exercise interventions (9,16,18) in which follow-up insulin sensitivity was measured at this time interval. The loss of this improvement among participants whose IVGTT was performed five days after exercise has been demonstrated in other studies (18), and seems to mirror the effect of stopping training among trained athletes (8,19,20). The 40% increase in insulin sensitivity seen within 24 hours of an exercise session in this trial is approximately the same as that which accompanies weight loss of 6-10% (7, 21). The Oslo Diet and Exercise Study (22) demonstrated more modest decreases in insulin resistance (measured by homeostatic modelling) of 9% with weight loss of 4.4% in the diet group, and a decrease of 20% with weight loss of 13% in the diet plus exercise group.

The precise frequency of exercise necessary to maintain increased insulin sensitivity cannot be determined from this study in which the increase is seen at 24 hours but not at five days. Other studies have found the effect to have worn off five days after exercise (18,19), but differ as to the effect at three days; King describing an increase maintained at three days (18), but Schneider, in Koivisto (9) not showing the same retention. The implications of our trial in the context of these smaller studies are that exercise training must be maintained for benefits in insulin sensitivity to be maintained.

CONCLUSIONS

We have demonstrated that a rigorous exercise programme undertaken by South Asians and Europeans can ameliorate insulin resistance. The improvement related to exercise is demonstrable 24 hours but not five days after an exercise session. Such an effect extrapolated to the population level would have important implications for reducing the risk of development of non-insulin-dependent diabetes.

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