Insulin sensitivity and fat mass in young male sedentary adults

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ABSTRACT

We live in an obesogenic environment, spending a lot of time sitting neglecting physical activity. This study aims to determine the impact of a sedentary lifestyle on insulin sensitivity by comparing insulin sensitivity of healthy athletes and sedentary subjects. Twelve athletes and 12 sedentary subjects underwent a two-step hyperinsulinemic euglycemic clamp test to assess insulin sensitivity and a DEXA scan to assess body fat mass. Insulin sensitivity was significantly lower in sedentary subjects (p=0.009) and fat mass negatively correlated with insulin sensitivity (r=-0.57, p=0.005). This study shows that healthy sedentary subjects have an impaired insulin metabolism compared to trained athletes.

Keywords

Obesogenic environment, insulin sensitivity, sedentary, athletes, body fat mass.

INTRODUCTION

We live in an obesogenic environment in which we are encouraged to eat unhealthy and where it is easy to relinquish physical activity. We are sitting at work, at home, in school and even at Universities, metabolic research takes place in a sitting position. A sedentary lifestyle and an unhealthy diet are considered to be the main factors leading to a positive energy balance. Obese and overweight people are called to be in positive energy balance where the calorie intake exceeds the calorie expenditure (1). In 2016 nearly 40% of the world's adult's population is overweight and 650 million are obese (2). Overweight and obesity are associated with secondary complications such as type two diabetes and cardiovascular diseases with possible lethal consequences. Nowadays we spent more time sitting compared to earlier generations and already a decrease in physical activity alone has been reported to have health consequences (3). A lot of physical intervention studies reported the beneficial effects of physical activity (4). However, the focus was rarely on the negative consequences of inactivity.

This study focuses on the difference in insulin sensitivity between sedentary subjects and endurance trained athletes. The second endpoint is to assess whether there is a correlation between fat mass and insulin sensitivity.

It is suggested that endurance trained athletes are more insulin sensitive then sedentary subjects. Furthermore, it is suggested that there is a negative correlation between insulin sensitivity and body fat mass.

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METHODS

Study design and subjects. Twenty-four participants were included within an observational cross-sectional study at Maastricht University. Twelve sedentary subjects and 12 endurance trained athletes were grouped on basis of a VO_2 max test (athletes >55ml min^{-1} kg^{-1} and sedentary <45 ml min^{-1} kg^{-1}). The subjects were recruited by Maastricht University announcing the research via flyers and newspapers. All subjects provided written informed consent to take part in the study.

Blood sample analysis. Blood samples taken during the clamp test, were immediately stored on ice and cold centrifuged (4°C) for 10 min at 2000RPM. Plasma was taken to determine glucose concentrations with enzymatic assays automated on the Cobas Fara/Mira (Roche Diagnostics, Basel, Switzerland) at the Department for Human Biology of Maastricht University.

VO_2 max test. The subjects underwent an incremental cycling test on an electronically braked cycle ergometer to determine VO_2 max and maximal workload capacity (Wmax) (Lode Excalibur, Groningen, The Netherlands). The performance was used to group the study population.

DEXA Scan. Total body fat mass, fat percentage and lean mass was measured by Dual energy X-rat absorptiometry (DEXA) in the fasted state (Lunar Prodigy; GE Healthcare, Milwaukee, MI).

Insulin sensitivity. Subjects underwent a two-step hyperinsulinemic euglycemic clamp test after an overnight fast. Subjects were instructed not to exercise 48h prior the test day. Two hours after injecting a [6,6 2H2] glucose tracer a low insulin infusion (10 mU/m^2/min) was administered followed by a high insulin infusion (40 mU/m^2/min). A variable 20% glucose – tracer solution was used to adjust fluctuations of blood glucose levels during clamping periods. The high insulin infusion phase was used to determine whole body insulin sensitivity, the primary outcome parameter of this study.

Calculations. The M – value is the golden standard to quantify insulin sensitivity and is applicable when the endogenous glucose production is assumed to be zero. For calculation of the M – value (μmol/kg/min) the glucose infusion rate (GIR) and a space correction (SC) was needed. The GIR describes the amount of glucose administered during the clamp and the SC corrects for glucose loss out of the glucose pool during steady state conditions.

Statistics. Data were presented as means and standard deviations (SD). A student's t – test and a Mann- Whitney U test was performed to assess statistical differences between the two groups. Correlation was tested using the Pearson correlation. Correction for confounding variables and testing interaction between variables was done with a backwards linear regression model. The significance level (α) was 0.05 and the working software IBM SPSS statistics 24 for Macintosh.

RESULTS

Subject characteristics. In total 23 participants took part in the study. One subject dropped out of the analysis due to missing results of the clamp test. Baseline characteristics of the subjects are reported in Table 1. Endurance trained subjects had a significantly higher VO2-Max (ml/min/kg) (p=0.000). Sedentary subjects had a significantly higher fat percentage and fat mass (p =0.013, p= 0.000, respectively).

Table 1. Baseline characteristics of untrained and trained subjects.

Parameter	Untrained Sedentary	Endurance Trained Athletes	P - value
n	11	12	
Age (years)	22.75 ± 3.25	25.42 ± 4.40	P= 0.193
Body mass (kg)	71.94 ± 6.44	72.42 ± 7.14	P= 0.950
Height (m)	1.84 ± 0.06	1.82 ± 0.05	P= 0.311
BMI (kg/m^2)	21.84 ± 1.93	21.36 ± 1.76	P= 0.325
Fasting Blood Glucose (mmol/L)	5.21 ± 0.33	5.05 ± 0.34	P= 0.090
Lean Body Mass (LMB)	56.57 ± 4.68	60.20 ± 5.73	P= 0.142
Fat Mass (kg)	13.92 ± 3.27*	9.56 ± 1.71	P= 0.000*
Fat Percentage (%)	18.05 ± 4.32*	13.14 ± 1.84	P= 0.013*
VO2-Max (ml/min/kg)	40.53 ± 2.40*	59.67 ± 3.48	P= 0.000*
Systolic BP (mmHg)	118.71 ± 10.34	119.21 ± 8.94	P= 0.970
Diastolic BP (mmHg)	73.00 ± 6.59	71.88 ± 6.80	P= 0.862

*BMI, Body mass index; BP, blood pressure; VO2-max, maximal oxygen consumption; *p<0,05 trained vs untrained. Values are expressed in means + SD, SD: Standard deviation.*

Difference in insulin sensitivity. In the low insulin infusion phase and in the high insulin infusion phase of the clamp test insulin sensitivity higher was higher in endurance trained athletes in comparison to sedentary subjects (p=0.001 and p=0.009 respectively) (Figure 1).

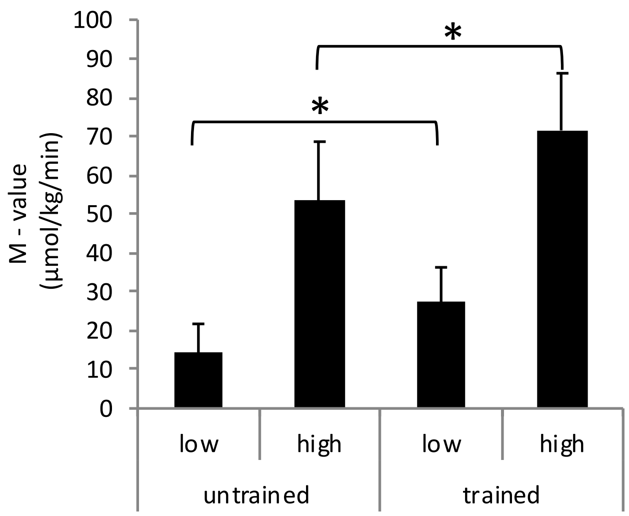

*Figure 1. Insulin sensitivity of sedentary and trained subjects in low and high insulin infusion phase during hyperinsulinemic euglycemic clamp test. Values are expressed in means + SD, SD: Standard deviation,*p<0,05 trained vs untrained*

Due to the significant baseline parameters fat mass, fat percentage and VO2 max (Table 1), a backwards linear regression model was implemented to control whether confounding variables influence whole body insulin sensitivity. Also, the group variable was included in the regression model. After implementing the model only fat mass was significantly influencing whole body insulin sensitivity (B = -2.759, p= 0.007).

Correlation fat mass and insulin sensitivity. A significant negative correlation between fat mass and whole body insulin sensitivity was found (r=- 0.57, p=0.005) (Figure 2).

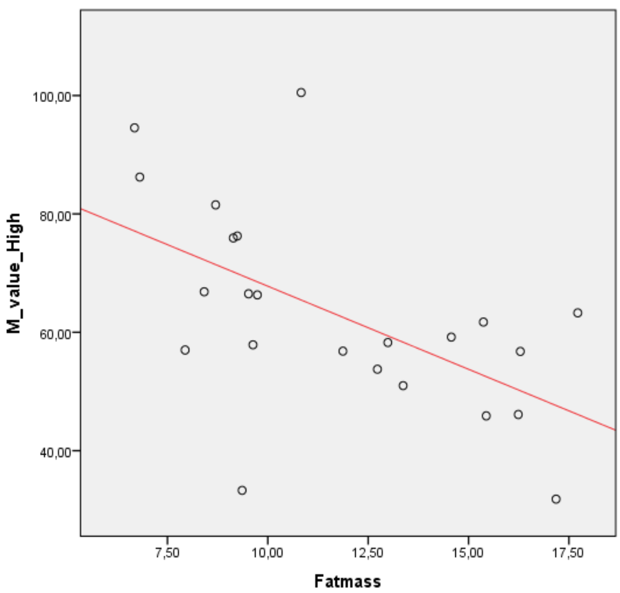

Figure 2. Significant, negative correlation between whole body insulin sensitivity (µmol/kg/min) and fat mass (kg) (r= -0,57, p<0,01).

Interaction training status and body fat mass. Furthermore, it was tested whether the variables group and fat mass together have and influence on whole body insulin sensitivity. A new variable 'groupfatmass' was created and implemented in a backwards linear regression model to assess its influence on insulin sensitivity. After running the model indeed, the new variable 'groupfatmass' and the group variable significantly influence whole body insulin sensitivity (p=0.001).

DISCUSSION

This study showed that sedentary subjects are significantly less insulin sensitive in comparison with endurance trained subjects. Furthermore, it was shown that there is a negative correlation between fat mass and insulin sensitivity.

In this study insulin sensitivity was assessed using a two-step hyperinsulinemic euglycemic clamp test. Physical activity is known to be the first and autonomous therapy to treat and prevent obesity and type two diabetes by enhancing insulin sensitivity. In a lot of studies it has been found that physical activity is positively associated with insulin sensitivity (5). Athletes are characterized by a higher peripheral blood flow and a larger diameter of blood vessels allowing more perfusion of metabolically active tissues (6, 7). However, there must be a mechanism leading to a more insulin sensitive tissue. It has been observed that exercise training is positively correlated to the amount of glucose transporter proteins, GLUT, shuttling glucose from the blood towards the cell (8). However, a mechanism why physical inactivity induces insulin resistance is not fully understood by now. Hamburg et al. conducted a study where 5 days of bedrest led to an increase in insulin response suggesting that inactivity is leading to insulin resistance (9). Animal studies showed that the lipoprotein lipase (LPL) activity is blunted in inactive rat hind limps in comparison to active controls (10). LPL, as an insulin regulated enzyme, plays an important role within lipoprotein metabolism. Deficits in LPL function are associated with a reduced capacity to clear lipids from the blood towards the tissues with the consequence of ectopic fat accumulation and deposition of lipids in arterial walls leading to the formation of arteriosclerotic plaques. On top of that, it has been found that the more time is spend sitting, insulin sensitivity decreases and the concentration of the inflammatory marker C – reactive protein (CRP) increases (11).

In this study it has been hypothesized that there is a negative correlation between body fat mass and insulin sensitivity. This study assessed body composition using a DEXA scan and found that there is a significant negative correlation between body fat mass and whole body insulin sensitivity. Other studies confirm that the amount of fat mass negatively correlates with insulin sensitivity. A study conducted by Kichhoff et al. found a negative correlation between total body fat and insulin sensitivity (12). Boden et al. reported similar findings were 6 elderly and 6 young healthy participants, matched for BMI, showed a negative correlation of body fat and glucose uptake (13). Recent literature also shows that sedentary behaviour is positively correlated to fat mass and waist circumference. On the other hand, it has been reported that moderate exercise leads to an decrease in fat mass after controlling for sedentary behaviour (14). These findings suggest that physical activity is crucial for sedentary people to stay metabolically healthy. Other studies report similar finding where it is concluded that already little daily physical activity has beneficial health effects.

A limitation but also strength of this study is that only healthy subjects were studied. It is therefore difficult to give a true reflection of the impact of body fat and insulin sensitivity in relation to the development of type two diabetes. However, it can be said that already healthy but sedentary subjects impairments in insulin sensitivity. Therefore, it is likely to interpret that sedentary people have an increased risk to gain body fat and become more insulin resistant.

Further studies can address the level of physical activity necessary to stay metabolically healthy and evaluate what kind of exercise is the most effective. It can also be beneficial to elaborate cut- off values for insulin resistance to evaluate a person's risk of the development of type two diabetes.

CONCLUSION

It is well known that physical activity has beneficial health effects in terms of decreasing body fat mass and decreasing the risk to develop insulin resistance and type two diabetes. However, it is also important to focus on the effects of physical inactivity on the glucose metabolism as recent research shows that inactivity is associated with impaired insulin resistance and an increase of body fat mass.

ROLE OF THE STUDENT

This research was performed during a Student Research Project of the BSc Biomedical Sciences at the Department for Human Biology at Maastricht University. The topic was proposed by the supervisor (Yvo op den Kamp). The student made use of this data set to analyze it in the way as reported in this paper. The data analysis and writing was performed by the student and discussed with the supervisor.

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