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Elucidating the minimum exercise requirements to overcome dietary-induced insulin resistance

F. J. Spargo[1], M. A. Febbraio[2], J. A. Hawley[1];
[1]Exercise Metabolism Group, RMIT University, Bundoora,
[2]Cellular and Molecular Metabolism Laboratory,
Baker Institute of Heart Research, Melbourne, Australia.

Background and Aims: During the past 50 years, the prevalence of a cluster of interrelated metabolic disease states including obesity, insulin resistance and type 2 diabetes mellitus has reached epidemic proportions. While there is irrefutable evidence that physical training is an effective therapeutic intervention to increase insulin action in skeletal muscle from obese and insulin resistant individuals, the minimum amount of exercise required to restore insulin tolerance is not known.
Materials and Methods: Thirty male Wistar rats (age ~9 wk) were fed standard chow (CHOW, n=6) or a 60% fat diet (FAT, n=24) for 6 wk. Fat-fed animals were then assigned to a control group (FAT, n=6) or one of three exercise groups; F100 (60 min/d for 6 d, n=6); F50 (50% volume of F100; 60 min/d for 3 d, n=6) or F25 (25% volume of F100; 30 mind for 3 d, n=6). 24 hr after the last exercise session trained animals, as well as CHOW and FAT controls underwent an intraperitoneal insulin tolerance test (IPITT), before the red gastrocnemius was removed for analyses.
Results: CS activity was higher in all fat-fed groups compared to CHOW (all P<0.05), while F50 CS activity was increased compared to FAT and F25. F100 CS activity was also increased compared to FAT, F25 and F50 (all P<0.05). Compared to FAT, IPITT was improved in all exercise groups (P<0.05). F100 also had greater insulin tolerance compared to both F25 and F50 (P=0.02; Figure 1A). FAT glycogen was lower than CHOW (P=0.03), F50 (P=0.05) and F100 (P=0.05), while F25 glycogen was lower than F100 (P=0.04). There were no intramuscular triglyceride (TGm) differences between CHOW, FAT and F25, however both F50 and F100 had higher TGm compared to all other groups (all P<0.05). There were no differences in total IRS1 or IRS1 tyrosine phosphorylation (relative to total IRS1). However, FAT, F25 and F50 had reduced IRS1-PI3 kinase association (relative to total IRS1) compared to CHOW and F100 (all P<0.05). FAT, F25 and F50 GLUT4 was lower than both CHOW and F100 (all P<0.05), while FAT GLUT4 was also lower than both F25 and F50 (both P<0.05).
Conclusion: Insulin tolerance was improved in fat-fed animals after all exercise interventions. However, only the largest exercise dose (60 min/d for 6 d) was sufficient stimulus to overcome high fat feeding-induced down-regulation of the insulin signalling pathway. These data suggest that in order to overcome dietary-induced insulin resistance, daily moderate intensity activity of ~1 hr duration is recommended. (Fig. 1)

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Lifestyle-induced changes in transferrin are associated with changes in insulin sensitivity

E. E. Blaak[1], C. Roumen[1], E. J. M. Feskens[2], W. H. M. Saris[1];
[1]Human Biology, Maastricht University,
[2]Division of Human Nutrition, Wageningen University, The Netherlands.

Background and Aims: Indicators of iron status, like transferrin and ferritin levels may be related to diabetes risk. Ferritin and transferrin may be independent predictors of insulin resistance. Less is known on whether lifestyle intervention can improve serum levels of transferrin and ferritin. We evaluated the effect of a lifestyle intervention in a Dutch population with impaired glucose tolerance (IGT) and analysed the relationship between lifestyle-induced changes glucose tolerance, and insulin sensitivity and changes in transferrin and ferritin levels.
Materials and Methods: 147 IGT subjects were initially randomised into an intervention group; n=74 (INT) and control group; n=73 (CON). We studied 129 subjects after one year of study (INT n=64 and CON n=65). Subjects underwent measurements of body composition, body fat distribution, glucose tolerance (OGTT), and maximal aerobic capacity (VO_2 max). INT were individually guided with respect to diet and physical activity, based on general public health recommendations. We used simple linear regression to evaluate the relationship between lifestyle-induced changes in glucose tolerance, and insulin sensitivity and changes in transferrin and ferritin levels. We used stepwise and multiple linear regression to evaluate whether changes in transferrin were independently related to changes in insulin resistance (as assessed by HOMA-IR).
Results: INT decreased more in body weight and 2-hr glucose levels than CON, −2.32±0.45 kg vs.0.59±0.47 kg (p=0.009) and −0.63±0.22 mM vs. 0.25±0.27 mM (0.014). VO_2 max increased more in INT compared to CON (p=0.033). HOMA-IR tended to decrease more in INT compared to CON (p=0.075). At baseline, transferrin and ferritin were negatively associated (β= −0.524, p<0.001) and lifestyle-induced changes in these parameters were also negatively associated (β= −0.253, p=0.004). The lifestyle-induced decrease in fasting and 2-hr insulin and HOMA-IR were positively associated with decrease in transferrin (p<0.05), but not with ferrtitin (p>0.05). Multiple linear regression revealed that the change in transferrin was related to the change in HOMA-IR (β=0.143, p=0.044), independent of changes in body mass index, age and sex with these factors accounting for 44.6% of the variation. Stepwise linear regression analysis adjusted for age and sex revealed that the most important predictors of change in HOMA-IR were change in BMI (β =0.640, p<0.001) and change in transferrin (β=0.144, p=0.035).
Conclusion: Transferrin and ferritin were negatively associated and did not change between INT and CON. Transferrin appeared to be an important independent determinant of the improvements in insulin sensitivity. These data suggest that the iron metabolism may be involved in the development of insulin resistance and type 2 diabetes.
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Fig. 1