

The Effects of Exercise and a Low-Fat Diet on Monocyte TLR Expression and Disease Risk in Mice.

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Excess adiposity increases systemic inflammation, which is implicated in various diseases. Physical activity is a common treatment to reverse weight gain and increased disease risk; however, little evidence is available to determine if forced or voluntary exercise is more effective in mice. Such information has implications for the refinement of human exercise interventions. **PURPOSE:** To determine if 8-weeks of exercise combined with low-fat feeding reverses changes in disease risk, monocyte concentration and monocyte TLR2/TLR4 expression. **METHODS:** For 12-months, 24 CD-1 mice underwent pre-treatment, consuming either a low-fat (10% kcal from fat, N=6) or high-fat (60% kcal from fat, N=18) diet *ad libitum*. High-fat fed mice were randomly assigned to one of three groups (N=6/group): V-EX (low-fat chow, access to running wheel 5 d/week), F-EX (low-fat chow, forced treadmill running at 22 m/min, 60-min/d, 5 d/week), or SD (low-fat chow, no exercise). Mice pre-treated with low-fat chow served as controls (CN, N=6). Measurements were made on weekly saphenous vein blood samples using 3-color flow cytometry. Blood glucose and cholesterol concentration were analyzed weekly using a glucose and cholesterol analyzer. IPGTT was performed at baseline and week 8 and analyzed as area under the curve. **RESULTS:** All groups lost significant body weight over 8-weeks ($P<0.001$). V-EX ran 4.4x more than F-EX ($P<0.001$). There were no significant effects for blood cholesterol. CN had 26% higher glucose levels than V-EX ($P=0.009$). On average, there was a 59% decrease in IPGTT AUC from baseline to week 8 and V-EX decreased 37% more than CN. At week 8, monocyte concentration was 6x higher than week 1 ($P=0.002$). Specifically, V-EX was greater than both CN (49%) and F-EX (59%). Cell-surface TLR2 expression was significantly greater at week 6 (55%) and week 8 (23%) relative to baseline. Monocyte cell-surface TLR4 expression increased from baseline to week 8 ($P<0.001$). **CONCLUSIONS:** Combining low-fat diet and exercise caused significantly more weight loss than low-fat diet alone. Overall, there was decreased insulin resistance and decreased glucose, suggesting there may have been a decrease in type II diabetes risk. Lack of difference in monocyte concentration and TLR2/4 cell-surface expression suggest the diet and exercise intervention was not long enough to elicit changes in inflammation following the long-term high-fat feeding. More research is needed to understand the time course of these changes. This study was useful in understanding what occurs during a diet and exercise intervention and in directly comparing forced and voluntary exercise.