Voluntary Exercise Causes Greater Weight Loss in Obese Mice

KC Carpenter, K Strohacker, WL Breslin, MR Morrison, J Potucek, N Agha, RJ Simpson, T Lowder, BK McFarlin

University of Houston

BACKGROUND: Diseases resulting from overweight and obesity, such as Type 2 Diabetes Mellitus, CVD, hypertension, and many others, are on the rise in the United State [1]. Increases in the number of people affected by chronic long-term weight gain may be to blame. The most common cause of weight gain is excessive caloric intake coupled with a decrease in physical activity, which results in a positive energy balance. Excess adiposity is a result of weight gain, which is known to lead to a state of chronic, systemic, low-level inflammation [2]. Inflammation is known to cause elevated levels of blood glucose, fatty acids, and cholesterol, which are all important risk factors for disease [2]. Exercise has anti-inflammatory effects on the body, which makes it an effective treatment to counter diet-induced weight gain [3]. In mice, most studies use forced exercise as a means of exercise intervention; however, there has been some debate as to whether this causes unnecessary stress, thus causing increased cholesterol and inflammation [4]. Voluntary exercise, on the other hand, may be less stressful since the individual gets to choose the intensity and duration of the exercise [4]. In murine research, voluntary exercise protocols have a benefit that mice have the tendency to run spontaneously throughout their day, rather than be forced to exercise for a given amount of time; forcing mice to run on a treadmill removes them from their normal behavior [5].

PURPOSE: The primary purpose was to determine if 8-weeks of aerobic exercise training combined with a low-fat diet would reverse the changes in body weight, cholesterol, glucose, and glucose tolerance area under the curve associated with 12-months of high-fat feeding. The secondary purpose was to compare and contrast voluntary wheel running and forced treadmill running.

METHODS: For 12-months, 24 CD-1 mice underwent a pre-treatment feeding phase, consuming either a low-fat (10% kcal from fat) or high-fat (60% kcal from fat) diet *ad libitum*. Prior to pre-treatment, the mice were randomly assigned to one of four groups (N=6/group) based on diet composition and exercise prescription: CN (consumed low-fat chow for 12-months and duration of study, no exercise), V-EX (consumed high-fat chow for 12-months, switched to low-fat chow, were allowed free access to running wheel 5 days/week), F-EX (consumed high-fat chow for 12-months, switched to low-fat chow, and underwent forced treadmill running at 22 $m\text{-}min^{-1}$ for 60-min/day, 5 days/week), or SD (consumed high-fat chow for 12-months, switched to low-fat chow, no exercise). Body weight was measured daily using a digital scale. Total blood cholesterol and blood glucose were measured weekly using commercially available monitoring systems. IP glucose tolerance tests were performed at baseline and week 8, during which glucose was measured at 0, 15, 30, 60, and 120-min post IP injection of 1.5 $g\text{-}kg^{-1}$ of dextrose solution. Blood glucose concentration was determined and area under the curve was calculated as an index of insulin sensitivity.

RESULTS: In terms of body weight, all groups lost significant weight over the 8-weeks ($P<0.0001$). V-EX weighed 23.2±3.6 g less ($P<0.0001$) and F-EX weighed 17.3±3.4 g less ($P<0.0001$) at week 8 compared to baseline. The V-EX group ran significantly more, 4.4x times the distance compared to F-EX, over the 8-weeks ($P<0.0001$). There were no significant effects for blood cholesterol. The CN group had 26% higher glucose levels than V-EX ($P=0.009$). No other significant effects for blood glucose were found. There was a 59.3% decrease in IP glucose tolerance between baseline and week 8 ($P=0.001$). V-EX decreased 37.4% more than CN over the 8-weeks ($P=0.023$).

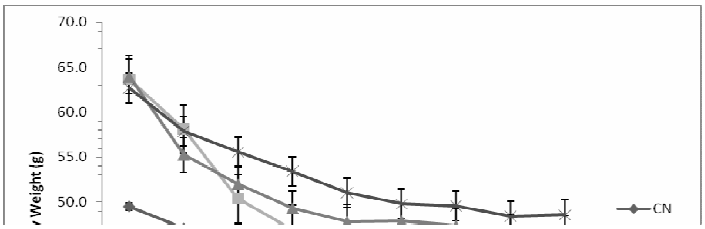

Figure 1: Body weight (g) prior to and during 8-weeks of treatment.

CONCLUSION: Consumption of a low-fat diet and exercise caused significant weight loss following 12-months of high-fat feeding. Voluntary exercise reversed the increases in glucose and insulin resistance from high-fat feeding. Since, V-EX ran significantly more than F-EX; more research is needed to determine whether it is the mode or distance that caused the changes.

REFERENCES:

1. Wyatt, S.B., K.P. Winters, and P.M. Dubbert, *Overweight and obesity: prevalence, consequences, and causes of a growing public health problem.* Am J Med Sci, 2006. **331**(4): p. 166-74.
2. Bastard, J.P., et al., *Recent advances in the relationship between obesity, inflammation, and insulin resistance.* Eur Cytokine Netw, 2006. **17**(1): p. 4-12.
3. McFarlin, B.K., et al., *Physical activity status, but not age, influences inflammatory biomarkers and toll-like receptor 4.* J Gerontol A Biol Sci Med Sci, 2006. **61**(4): p. 388-93.
4. Bradley, R.L., et al., *Voluntary exercise improves insulin sensitivity and adipose tissue inflammation in diet-induced obese mice.* Am J Physiol Endocrinol Metab, 2008. **295**(3): p. E586-94.
5. De Bono, J.P., et al., *Novel quantitative phenotypes of exercise training in mouse models.* Am J Physiol Regul Integr Comp Physiol, 2006. **290**(4): p. R926-34.