Reverting to a Healthier Diet or Employing an Aerobic Exercise Regime Independently Restore Muscle Fiber Phenotype Disturbed by High-Fat Diet in Muscle of Mice

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ABSTRACT

Obesity affects roughly 42% of the US population. High fat/high sugar diets (HFHS) often referred to as "western diet" contributes to this prevalence. Diet-induced obesity results in impaired metabolic responses and associated disease states (i.e., Type 2 Diabetes). Metabolic impairments in diet-induced obesity are a result of changes in muscle metabolism, and changes in muscle fiber phenotype, which is determined by the isoform-content of the protein myosin heavy chain (MHC). Fast muscle fiber phenotype (i.e. type IIb in mice) is characterized by lower capacity for utilization of lipids, implicated in the pathogenesis of Type 2 Diabetes. Regular exercise shifts MHC proportions under healthy circumstances. However, exercise-driven fiber type shifts in diet-induced obesity are less understood. **PURPOSE** To determine the impact of exercise and diet on fiber-type proportions in mice. We hypothesized that exercise would shift the mouse gastrocnemius muscle phenotype induced by a HFHS diet away from IIb fast fiber types. **METHODS** 49 C57BL/6 mice were split into 4 groups: 1) a Control (n = 9) fed a standard chow diet and water for 24 weeks, 2) a HFHS, fed a HFHS diet (60% of calories from fat, high sugar/fructose: 42 g/L in drinking water) for 24 weeks, 3) a HFHS Control (n = 10) fed a HFHS diet for 12 weeks followed by a standard chow diet and water for the next 12 weeks (i.e., simulating traditional dieting approach), and 4) a HFHS + exercise group fed a HFHS diet for 24 weeks, and performed aerobic exercise (30 minutes of treadmill running 5 days/week) in the last 12 weeks. Gastrocnemius muscles were collected, homogenized, and analyzed for MHC isoforms using SDS-PAGE. Intensity of bands corresponding to MHC IIa, IIx, and IIb isoforms were quantified using Image J (bands for the IIa and IIx isoforms were analyzed as a single band). Paired sample t-tests were conducted for differences between the MHC isoforms across groups. **RESULTS** Proportions of MHC IIb isoform increased (91 +/- 3%) in HFHS compared to the Control (81 +/- 6.2%, p=0.195), HFHS Control (77 +/- 3%, p=0.004), and HFHS + exercise groups (79 +/- 5%, p=0.057). Additionally, MHC IIa/x proportions in the HFHS (8+/-3%) compared to the Control (17 +/- 5.9%, p=0.184), HFHS Control (20 +/- 2%, p=0.004), and the HFHS + exercise (18 +/- 4%, p=0.054) groups was reduced. **CONCLUSION** These data suggest HFHS diet increases the proportion of IIb fibers and reduces IIa/x fibers in mouse gastrocnemius muscle over 24 weeks. Importantly, performing aerobic exercise with a HFHS diet or switching to a healthier diet restores the muscle fiber phenotype in mouse gastrocnemius muscle. Thus, exercise and dietary interventions may be a good strategy to shift MHC isoforms away from the extreme fast fiber phenotype, which has lower capacity for lipid utilization. Future research should determine single muscle fiber phenotype shifts related to long-term diet changes and exercise in humans to better understand regulation of muscle fiber phenotype and its impact on human metabolism.

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