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Modeling Energy Dynamics in Mice with Skeletal Muscle Hypertrophy Fed High Calorie Diets

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Retrospective and prospective studies show that lean mass or strength is positively associated with metabolic health. Mice deficient in myostatin, a growth factor that negatively regulates skeletal muscle mass, have increased muscle and body weights and are resistant to diet-induced obesity. Their leanness is often attributed to higher energy expenditure in the face of normal food intake. However, even obese animals have an increase in energy expenditure compared to normal weight animals suggesting this is an incomplete explanation. We have previously developed a computational model to estimate energy output, fat oxidation and respiratory quotient from food intake and body composition measurements to more accurately account for changes in body composition in rodents over time. Here we use this approach to understand the dynamic changes in energy output, intake, fat oxidation and respiratory quotient in muscular mice carrying a dominant negative activin receptor IIB expressed specifically in muscle. We found that muscular mice had higher food intake and higher energy output when fed either chow or a high-fat diet for 15 weeks compared to WT mice. Transgenic mice also matched their rate of fat oxidation to the rate of fat consumed better than WT mice. Surprisingly, when given a choice between high-fat diet and Ensure® drink, transgenic mice consumed relatively more calories from Ensure® than from the high-fat diet despite similar caloric intake to WT mice. When switching back and forth between diets, transgenic mice adjusted their intake more rapidly than WT to restore normal caloric intake. Our results show that mice with myostatin inhibition in muscle are better at adjusting energy intake and output on diets of different macronutrient composition than WT mice to maintain energy balance and resist weight gain.

Key Word :
Computational modeling, energy balance, fat oxidation, food intake, high-fat diet, myostatin, obesity, skeletal muscle hypertrophy.

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