ABSTRACT

There has been a precipitous decline in the daily physical activity in humans that has been accompanied by an epidemic rise in the incidence of obesity and type II diabetes. This rapid decline in physical activity in humans was simulated using a rat model where male rats that were physically active on voluntary running wheels for 21 days had their running wheels locked for 5-53 hours. During this time frame (between 5 and 53 hours of reduced physical activity), there is decreased insulin sensitivity in the epitrochlearis muscle, an increase in the mass of the epididymal and omental fat depots, and an increase in the size of epididymal adipocytes. In the epitrochlearis muscle, there was a decrease in multiple descriptive indices of insulin receptor activation that was associated with the decreased insulin sensitivity. In epididymal fat, there was an increase in triacylglycerol synthesis above that of animals that did not have access to running wheels; this was paralleled by an increase in the enzyme activity of mitochondrial glycerol-3-phosphate acyltransferase (GPAT), a key regulatory point in the triacylglycerol synthesis pathway. An increase in mitochondrial GPAT
protein is at least partly responsible for the increased enzyme activity. These studies provide a seminal foundation of mechanistic insights on how reduced physical activity elicits physiological changes that are commonly associated with common modern chronic diseases.