CALORIC RESTRICTION MODULATES ADIPONECTIN SIGNALING IN RAT ADIPOSE TISSUE

M. Zhu (P), R. DeCabo, D. K. Ingram

Laboratory of Experimental Gerontology, National Institute on Aging, National Institutes of Health, Baltimore, MD

Adipose tissue plays a crucial role in the regulation of insulin sensitivity and lipid metabolism. Reduction in plasma adiponectin levels in the prediabetic state precedes the decline in insulin sensitivity, contributing to insulin resistance and the development of Type 2 diabetes which are frequent complications of obesity. The peroxisome proliferator-activated receptor (PPAR)γis a critical transcription regulator involved in adipogenesis and insulin sensitivity. Our previous study focused on the role of adiponectin (ADP) in regulating energy homeostasis and insulin action in liver and muscle of caloric restricted rats. We found that circulating ADP levels were significantly increased by caloric restriction (CR). Increased plasma ADP levels in CR rats were accompanied by increased expression of the transcription factor mRNAs for PPAR α, γ, and δ, but decreased expression for SREBP-1c, resulting in a concerted modulation in the expression of key transcription target genes involved in fatty acid oxidation. In the present study, we addressed the hypothesis that CR increases circulating ADP levels via activation of PPARγ in adipose tissue. This pathway may represent an important mechanism in the anti-aging effects by CR. Using male F344 rats, we evaluated the effects of CR (40% from ad libitum for 2-25mo) on plasma factor profiling and mRNA levels for PPARγ and ADP, as well as the expression levels of ADP content in white adipose tissue (WAT). Moreover, we have examined the insulin receptor signaling in WAT. Our preliminary data in the present study demonstrated that CR rats exhibited a significant increase in adipogenesis via activated PPARγ, consistent with increased ADP in both circulation and WAT. Increased adiponectin may contribute to a decline in tissue triglyceride accumulation via a concerted modulation in the expression of key transcription target genes involved in fatty acid oxidation, thereby improving insulin receptor signing in peripheral tissues.