The effects of aging on mitochondrial biogenesis and insulin action in adipose tissue

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ABSTRACT

Mitochondrial biogenesis in skeletal muscle has been shown to decrease with age, a process which may cause the impairment of insulin signal transduction and age-related insulin resistance. In the current study, the effects of age on *in vivo* insulin action, insulin signaling, and mitochondrial biogenesis in adipose tissue were studied. Adipose tissue is an insulin-sensitive tissue that plays a role in the development of insulin resistance. However, it is not known if mitochondrial biogenesis in adipose tissue contributes to insulin resistance. *In vivo* insulin action was assessed by an insulin-assisted glucose tolerance test and was significantly reduced in aged (AG) mice compared to young (YG) controls, indicating insulin resistance. Insulin signal transduction via the phosphatidylinositol 3-kinase/AKT pathway was assessed by investigating the AKT/PKB protein intermediate. Phosphorylation of AKT/PKB on Thr^{308}, a surrogate measure of AKT/PKB activity, was significantly higher in AG mice, suggesting increased insulin signal transduction despite increases in whole-body insulin resistance. Total expression of AKT1/PKBα and AKT2/PKBβ were not significantly different between AG and YG mice, demonstrating that the increase in AKT/PKB activity was not accompanied by increases in gene expression. These findings indicate that *in vivo* insulin resistance can occur with an increase in insulin signal transduction measured at AKT/PKB, suggesting impairment of the insulin pathway occurs at downstream intermediates. Expression of the key transcription factor co-activator for mitochondrial gene transcription, PGC-1α, was used as a marker of mitochondrial biogenesis and showed a trend towards increasing in the AG mice, indicating increased mitochondrial biogenesis with age. In summary, advancing age results in insulin resistance without a decline in either insulin signaling or mitochondrial biogenesis.