TACSM Abstract

Geranylgeraniol Increases Autophagy and Mitophagy Gene Expression in Soleus of Rats with Diabetes

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ABSTRACT

The autophagy and mitophagy (selective autophagy for mitochondria) processes are important in maintaining muscle homeostasis, e.g., removing damaged mitochondria. With diabetes, skeletal muscle autophagy decreases. Geranylgeraniol (GG) has been shown to reduce mitochondrial damage; however, the effect of GG on basal autophagy and mitophagy in diabetic rats is not known. **PURPOSE**: To determine the effect of GG on selective autophagy and mitophagy genes in rats with diabetes induced by a high-fat diet (HFD) with streptozotocin (STZ). **METHODS**: Sprague-Dawley rats were divided into three groups: normal diet (CON; n=11), HFD with 35 mg/kg body weight of STZ (HFD; n=9), and HFD/STZ with 800 mg/kg body weight of GG (GG; n=9). On the 7th week, soleus muscles were collected and analyzed for gene expression of LC3A, LC3B, P62, PINK1, PARKIN, DRP, and MFN. Gene data were normalized to CON. **RESULTS**: A significant ($p < 0.05$) condition effect was found for autophagy (LC3A, LC3B, and P62) and mitophagy (PINK1, DRP, and MFN) gene expression. For autophagy, HFD (0.14 ± 0.03-fold) had significantly lower LC3A than CON (1.00 ± 0.22-fold), lower LC3B (0.67 ± 0.26-fold vs. 2.37 ± 0.72-fold) and P62 (0.44 ± 0.13-fold vs. 1.70 ± 0.35-fold) than GG. HFD trended to have lower LC3A than GG (0.14 ± 0.03-fold vs. 0.86 ± 0.26-fold; $p = 0.066$) while CON trended to have lower LC3B than GG (1.00 ± 0.07-fold vs. 2.37 ± 0.72-fold; $p = 0.078$). For mitophagy, HFD (0.32 ± 0.07-fold) and GG (0.51 ± 0.15-fold) had significantly lower PINK1 than CON (1.00 ± 0.13-fold). Further, HFD had lower MFN than GG (0.31 ± 0.08-fold vs. 1.46 ± 0.25-fold) and lower DRP than CON (0.48 ± 0.11-fold vs. 1.00 ± 0.15-fold). HFD trended to have lower PARKIN than GG (0.46 ± 0.08-fold vs. 1.38 ± 0.38-fold; $p = 0.053$) with no difference between GG and CON. **CONCLUSION**: In comparison to HFD, GG consumption improved the basal transcript abundance of the selective skeletal muscle autophagic and mitophagic genes, which could indicate an increased capacity to remove damaged mitochondria in diabetic rats.