Chronic Binge Alcohol-Induced Dysregulation of Mitochondrial-Related Genes in Skeletal Muscle of Simian Immunodeficiency Virus-Infected Rhesus Macaques at End-Stage Disease

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Abstract

Aims

Alcohol use disorders are more prevalent in HIV patients than the general population. Both chronic alcohol consumption and HIV infection have been linked to mitochondrial dysregulation; and this is considered an important mechanism in the pathogenesis of muscle myopathy. This study investigated if chronic binge alcohol (CBA) administration impairs the expression of genes involved in mitochondrial homeostasis in SIV-infected macaques.

Methods

Male rhesus macaques were administered daily CBA (to achieve peak blood alcohol concentrations of 50–60 mM within 2 h after start of infusion) or sucrose (SUC) intragastrically 3 months prior to intravenous SIV_{mac251}inoculation and continued until macaques met criteria for end-stage disease. Skeletal muscle (SKM) samples were obtained at necropsy. Muscle samples were obtained from a cohort of healthy uninfected macaque controls and used for comparison of analyzed variables. Total RNA was extracted and gene expression was analyzed by quantitative polymerase chain reaction.

Results

The relative expression of peroxisome proliferator-activated receptor gamma coactivator-1 beta (PGC-1β) was significantly decreased in the SKM of CBA/simian immunodeficiency virus (SIV) macaques compared to uninfected controls ($P < 0.05$). SIV infection resulted in a significant upregulation ($P < 0.05$) of mitophagy-related gene expression, which was prevented by CBA. CBA suppressed expression of anti-apoptotic genes and increased expression of pro-apoptotic genes ($P < 0.05$).

Conclusions

These findings suggest that SIV infection disrupts mitochondrial homeostasis and when combined with CBA, results in differential expression of genes involved in apoptotic signaling. We speculate that impaired mitochondrial homeostasis may contribute to the underlying pathophysiology of alcoholic and HIV/AIDS associated myopathy.

Short summary

This study investigated if CBA administration dysregulates gene expression associated with mitochondrial homeostasis in the SKM of SIV-infected macaques. The results suggest that SIV infection disrupts mitochondrial homeostasis and when combined with CBA, results in differential expression of genes involved in apoptotic signaling.