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"Chronic binge alcohol and gonadal hormonal loss impair glucose-insulin dynamics in SIV-infected female rhesus macaques"

Background: The majority of people living with HIV (PLWH) are taking antiretroviral therapy (ART), meaning that they have an increased life expectancy but also an increased risk for chronic conditions such as metabolic dysregulation. Macaques (*Macaca mulatta)* infected with simian immunodeficiency virus (SIV) and treated with an ART regimen have shown to be an effective model for studying HIV disease progression. Previous studies demonstrate that chronic binge alcohol (CBA) leads to metabolic dysregulation in male macaques. The aim of this project is to determine the effect of CBA and gonadal hormone loss on glucose-insulin dynamics and pancreatic integrity in SIV-infected female rhesus macaques.

Methods: Animals were randomized to receive either daily water (VEH) or intragastric ethanol (CBA), infected with SIV, and treated with ART. Animals were then randomized into either receiving a sham surgery (SHAM) or an ovariectomy (OVX). Using a modified frequently sampled intravenous glucose tolerance test (FSIVGTT), blood glucose and serum insulin values were measured. Glucose and insulin dynamic measures were determined using minimal model (MINMOD), such as the acute insulin response to glucose (AIRg), insulin sensitivity (Si), disposition index (DI), and glucose effectiveness (Sg). To characterize pancreatic integrity, insulin and glucagon expression was determined in formalin-fixed, paraffin-embedded tissue. Corrected total cell fluorescence and islet size were calculated using ImageJ software.

Results: FSIVGTT demonstrated that both CBA ($p = 0.04$) and OVX ($p = 0.02$) had a main effect to reduce insulin area under the curve (AUC). There were no significant differences in glucose values between the SHAM animals, but CBA significantly increased glucose AUC ($p = 0.01$) in OVX animals. CBA had a main effect to reduce AIRg ($p = 0.03$) and there were no differences in the Si, DI, or Sg. Glucagon expression was significantly lower in both groups, but there were no significant differences in either insulin or glucagon expression between groups. Of note, islet size in the CBA animals tended to be smaller, although non-significant ($p = 0.07$).

Conclusion: Gonadal hormone loss alters insulin and glucose values as determined by an intravenous glucose tolerance test. Chronic binge alcohol decreases the acute insulin response to glucose, although it does not alter basal expression of either insulin or glucagon. qPCR will be used to determine alterations in the expression of mRNA involved in pancreatic β-cell maintenance.