

POSTER 109

INTRINSIC HIGH AEROBIC CAPACITY PROTECTS AGAINST LIPID INDUCED HEPATIC INSULIN RESISTANCE

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Hepatic steatosis is commonly linked to hepatic insulin resistance. However, recent studies have found that increased hepatic triacylglycerol (TAG) accumulation is not always associated with impaired hepatic insulin signaling, leading to a hypothesis that partitioning of lipids into TAG in the liver matched with high rates of fatty acid oxidation (FAO) under high lipid exposure conditions may protect against hepatic insulin resistance. We examined this hypothesis in the livers of high and low capacity running (HCR/LCR) rats which were created by artificial selection based on differences in intrinsic aerobic capacity. We examined FAO, TAG storage, and insulin signaling in primary hepatocytes isolated from the HCR/LCR rats to determine if these factors are associated with protection or susceptibility to hepatic insulin resistance. HCR primary hepatocytes demonstrate 2-fold higher FAO to CO₂ than LCR, which is further increased following overnight lipid incubation. Also, HCR primary hepatocytes display 50% lower basal TAG synthesis rates and, unlike the LCR hepatocytes, demonstrate a 4-fold increase in TAG synthesis rate following overnight lipid exposure. Interestingly, overnight lipid exposure leads to the same TAG levels for both HCR and LCR hepatocytes. Finally, HCR hepatocytes are observed to maintain insulin stimulated Akt phosphorylation following overnight lipid exposure, with a significant decrease in signaling observed in the LCR hepatocytes. In conclusion, isolated primary hepatocytes from HCR rats are observed to have higher FAO, dramatically increased TAG synthesis rate, and maintenance of insulin signaling in response to lipid exposure. These data suggest that coupling of increased hepatic FAO and TAG synthesis in response to increased lipid exposure is protective of hepatic insulin action.