Non-alcoholic fatty liver disease and erectile dysfunction in S-nitrosoglutathione reductase (GSNOR) deficiency.

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Introduction

Recent animal and human studies link non-alcoholic fatty liver disease (NAFLD) to male sexual dysfunction, however, molecular and physiologic mechanisms correlating these conditions are incompletely established at this time.

Objectives

Since GSNOR is an important liver enzyme protecting against Western diet (WD)-induced erectile dysfunction (ED), we examined its potential concomitant effects on development and progression of NAFLD.

Methods

Male wild type and GSNOR$^{-/-}$ (mutant) mice were fed either a control diet (CD) or a WD (high fat and sugar content) for 3, 6, 9 or 12 weeks. All mice were studied at 20 weeks of age. Intra-cavernosal pressure (ICP) was measured at 1, 2, and 4 Volts electrical stimulation. Once mice were sacrificed at end of experiments, liver tissue was procured and preserved for histological examination. H&E-stained slides were blindly examined and scored by an experienced liver pathologist.

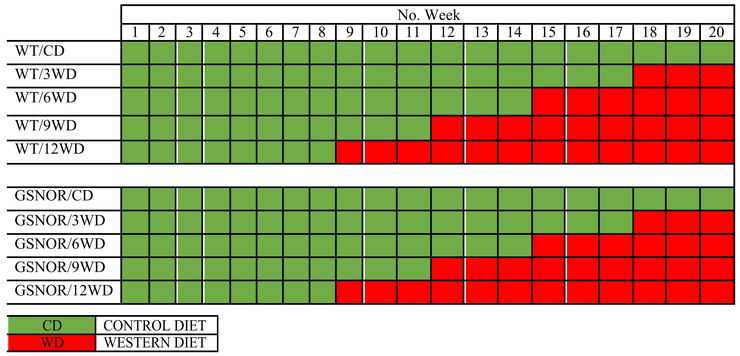

Figure 1. Study design – animal feeding schedule

Results

Electrical stimulation induced ICP responses revealed no difference in erectile function between WT and GSNOR$^{-/-}$ mice fed the CD. At nine weeks of WD, all animals developed ED, however those with GSNOR deficiency had a significantly worsened ICP values (p-value = 0.05). (Figure 2)

GSNOR$^{-/-}$ mice fed CD had worse liver scores at baseline, when compared to wild type animals, irrespective of the diet type. The liver dysfunction score in GSNOR$^{-/-}$ mice doubled following 9 weeks of WD. (Figure 3)

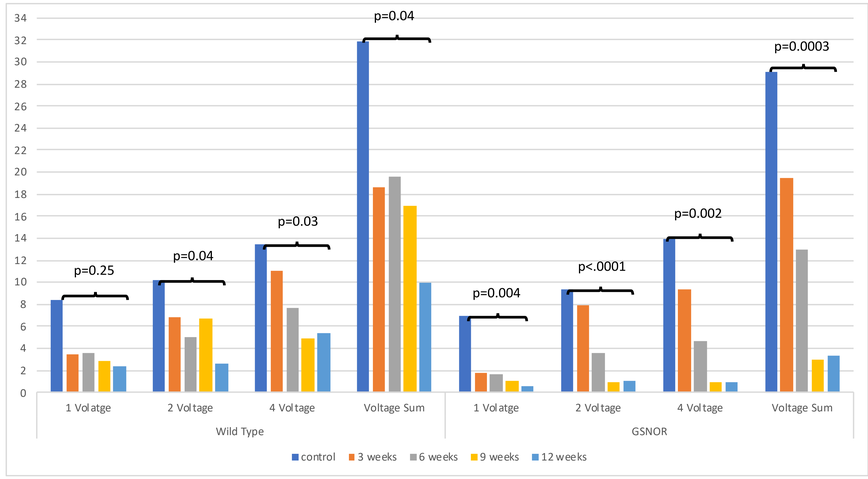

Figure 2. ICP responses according to the feeding schedule

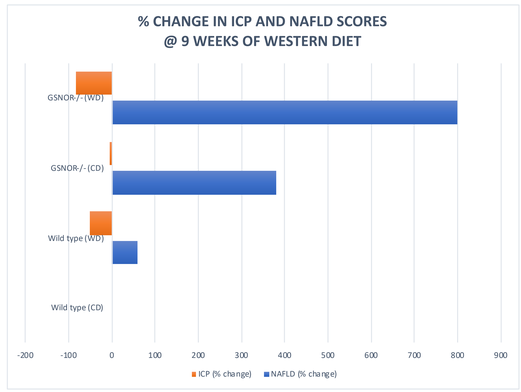

Figure 3. % change in ICP and NAFLD scores @ 9 weeks of Western diet

Conclusions

This study demonstrates a likely relationship of NAFLD and ED in animals fed Western Diet and elucidates need to fully examine their molecular, physiologic and clinical correlates.

GSNOR deficiency appears to be an important factor predisposing to both liver and erectile dysfunction, regardless of the dietary choices.

Additional work is necessary to fully examine underlying complex molecular relationships as they relate to NAFLD and ED development and progression.