SEX-RELATED FEATURES OF OXIDATIVE STRESS IN THE LIVER OF RATS WITH EXPERIMENTAL METABOLIC SYNDROME AND ITS CORRECTION WITH CARBACETAM

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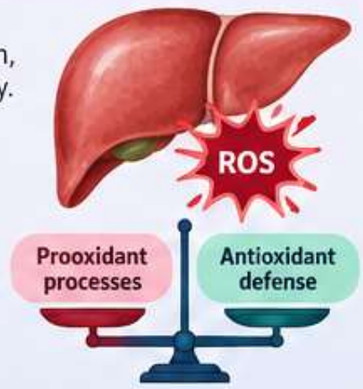
BACKGROUND

- Metabolic syndrome (MetS) is associated with disturbances in carbohydrate and lipid metabolism, which contribute to oxidative stress and liver injury.
- An imbalance between free radical oxidation and the antioxidant defense system plays an important role in these processes.
- Sex-related differences in these changes and the potential for their pharmacological correction using GABA receptor modulators require further investigation.



OBJECTIVE

To determine sex-related differences in changes in the hepatic prooxidant–antioxidant system in rats with experimental metabolic syndrome and to evaluate the effect of carbacetam on the extent of oxidative damage to cellular structures.

MATERIALS AND METHODS

Sexually mature albino rats (220–250 g)



Induction of metabolic syndrome (60 days)



High-calorie, high-fat diet with free access to 10% fructose

Treatment (14 days)



Carbacetam 5 mg/kg i.p.

Determined in the cytoplasmic fraction of liver tissue:

- Thiobarbituric acid-reactive products (TBARPs)
- Protein oxidative modification products at 370 nm (POM_{370}) and 430 nm (POM_{430})
- Activities of superoxide dismutase (SOD) and catalase

Statistical analysis:

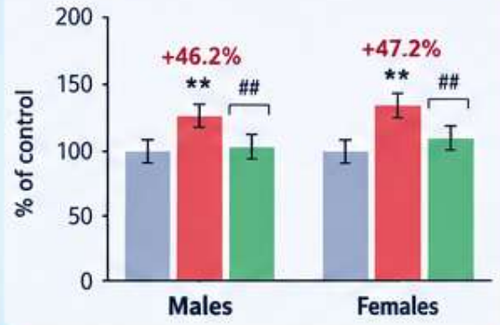
Student's t-test

RESULTS

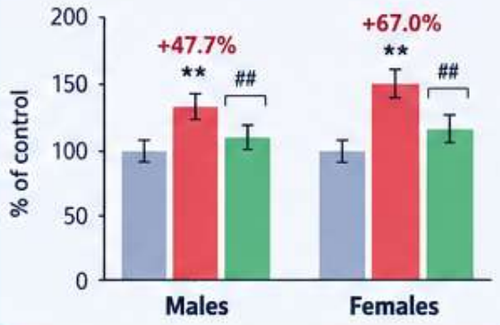
Control | Metabolic syndrome (MetS) | MetS + Carbacetam

Compared with control: * $p < 0.05$ ** $p < 0.01$ | Compared with MetS: # $p < 0.05$ ## $p < 0.01$

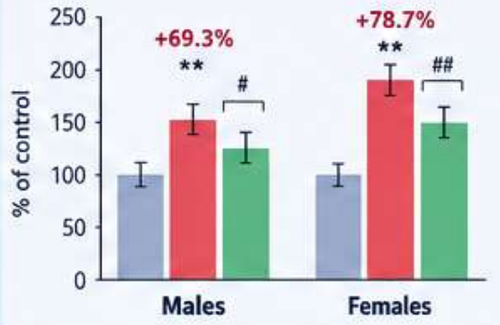
POM_{370} (protein oxidative modification)



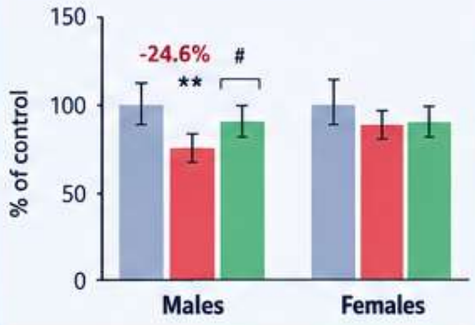
POM_{430} (protein oxidative modification)



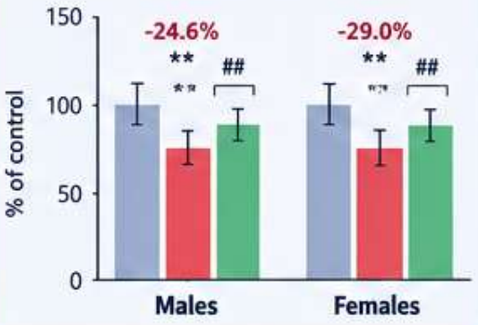
TBARPs (lipid peroxidation)



SOD activity



Catalase activity



MAIN FINDINGS

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- MetS increased POM_{370} by 46.2%, POM_{430} by 47.7%, TBARPs by 69.3%.
- Catalase activity decreased by 24.6%.
- SOD activity significantly decreased.

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- MetS increased POM_{370} by 47.2%, POM_{430} by 67.0%, TBARPs by 78.7%.
- Catalase activity decreased by 29.0%.
- More pronounced accumulation of protein and lipid oxidative damage compared with males.

Effect of carbacetam (5 mg/kg, 14 days)

- Reduced POM_{370}: –20.5% (males), –20.1% (females).
- Reduced POM_{430}: –23.8% (males), –28.3% (females).
- Reduced TBARPs: –15.1% (males), –20.3% (females).
- Increased catalase activity: +25.4% (males), +26.7% (females).
- Partial recovery of SOD activity in males.
- Investigated parameters did not return completely to control levels.

CONCLUSIONS

1. Experimental metabolic syndrome disrupts the prooxidant–antioxidant balance in the liver of rats of both sexes, as evidenced by increased lipid peroxidation and protein oxidative modification, together with decreased antioxidant enzyme activity.
2. Females exhibited more pronounced accumulation of products of oxidative damage to proteins and lipids.
3. Carbacetam administration at a dose of 5 mg/kg for 14 days provides partial correction of biochemical markers of oxidative stress, supporting further investigation of its antioxidant potential under conditions of metabolic disturbances.

Keywords: metabolic syndrome, liver, oxidative stress, lipid peroxidation, protein oxidative modification, carbacetam, sexual dimorphism.