FRUCTOSE INTAKE IN PREGNANCY AFFECTS ONE-CARBON METABOLISM OF FEMALE PROGENY

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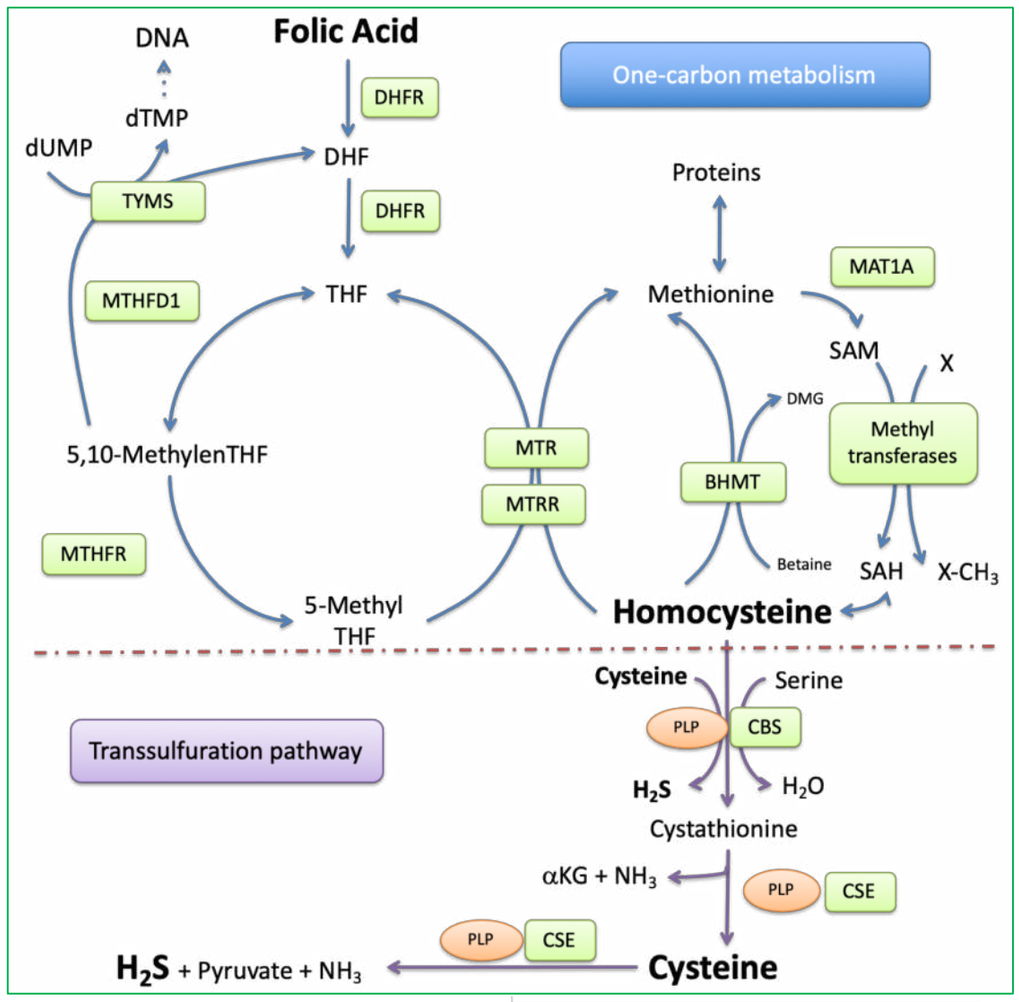
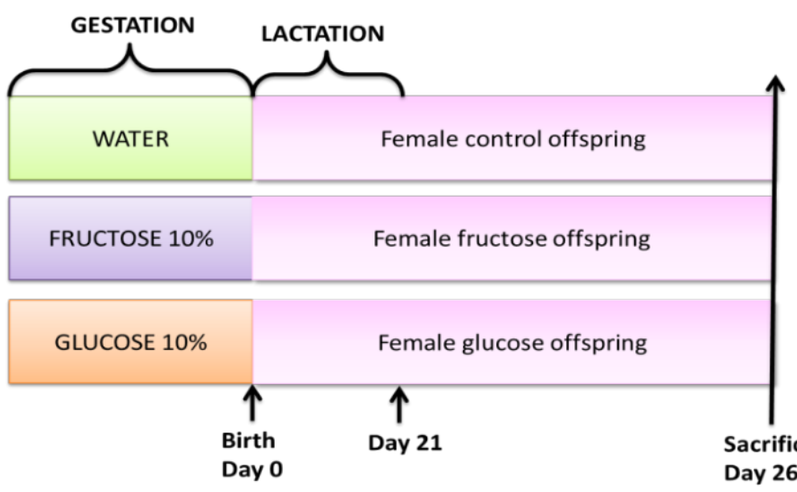
INTRODUCTION

Fructose consumption from added sugars correlates with the epidemic rise in obesity, metabolic syndrome and cardiovascular diseases. Fructose is a lipogenic substrate, because it is able to enter the glycolytic pathway bypassing the strictly regulated phosphofructokinase-1 step. It has been demonstrated that fructose intake during pregnancy affects offspring's health, and this is why our aim is to study whether maternal fructose intake produces subsequent changes in one-carbon metabolism and transsulfuration pathways on female progeny.



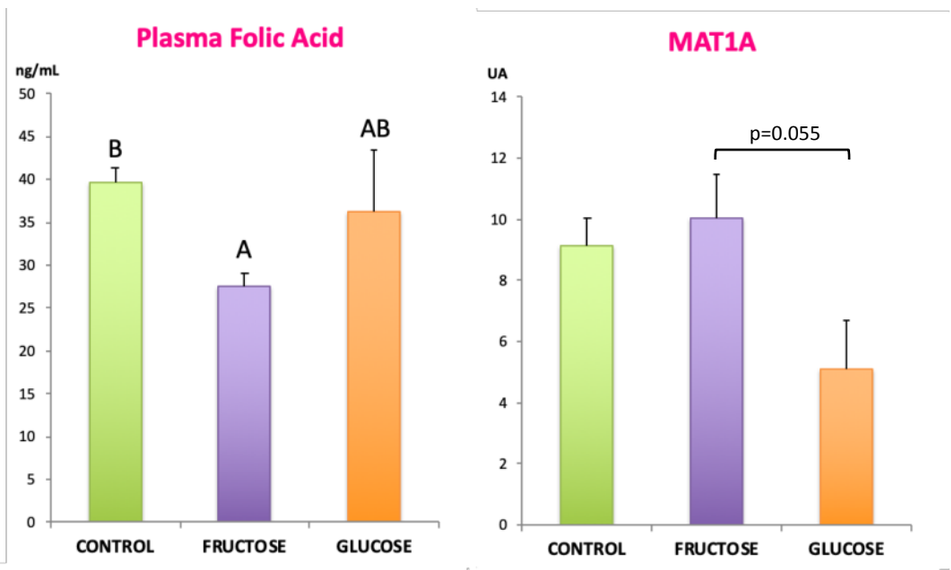
MATERIALS AND METHODS

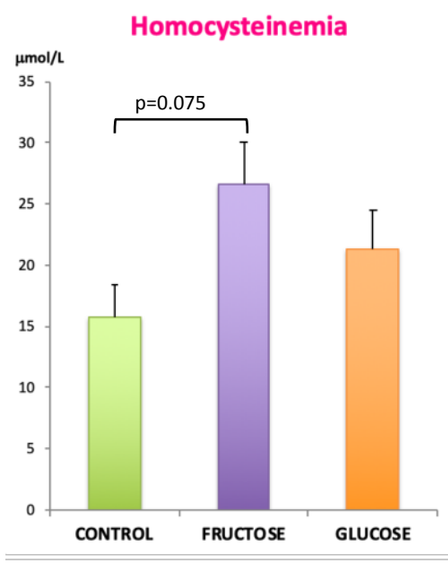


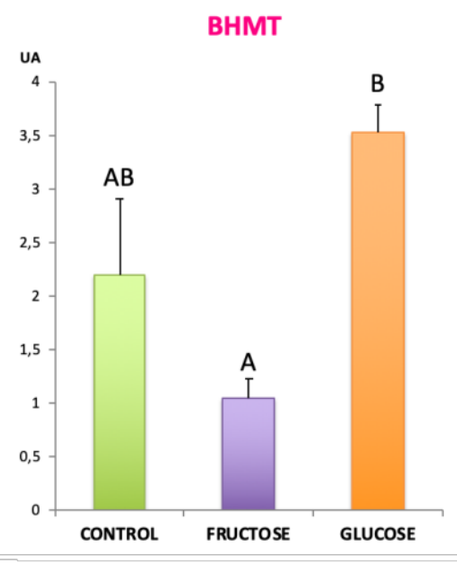
Plasma measurements: Folic acid, Homocysteine, Hydrogen sulfide (H_2S)

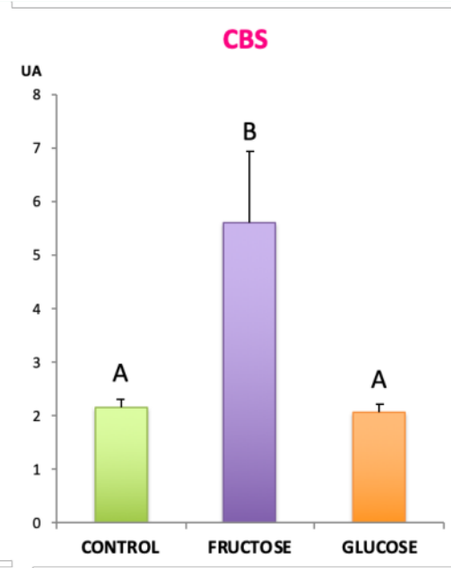
Liver Gene Expression (MAT1A, MTR, MTFHR, BHMT, CBS, CSE), **DNA methylation (**LXRα, CPT1), **protein carbonylation and H_2S production**

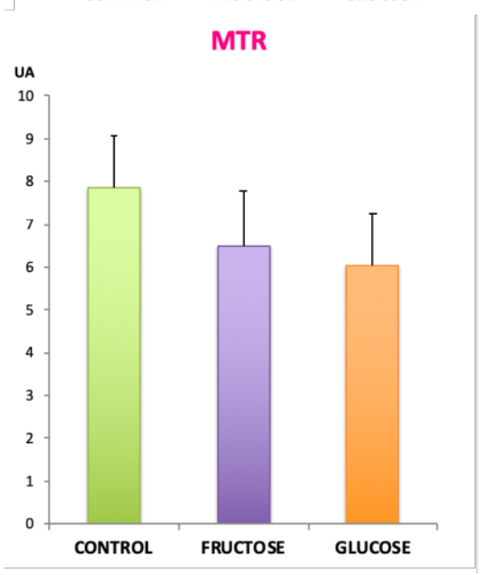
RESULTS

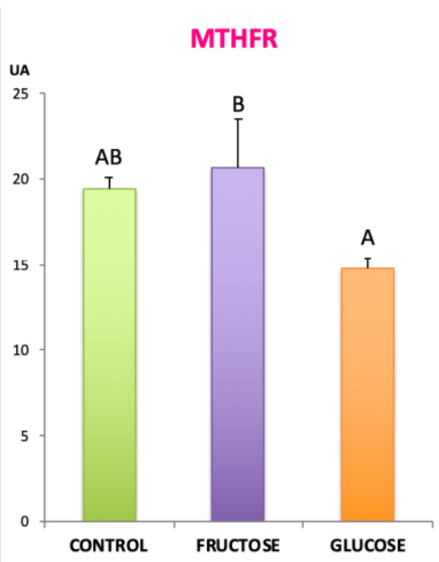


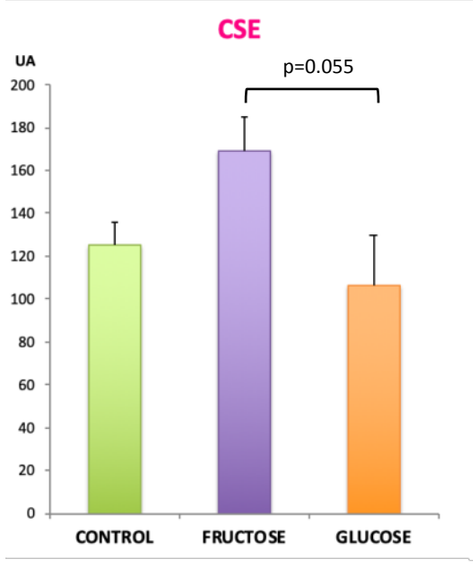


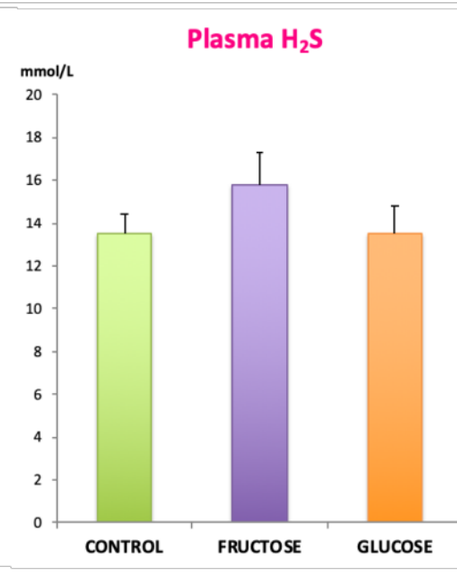


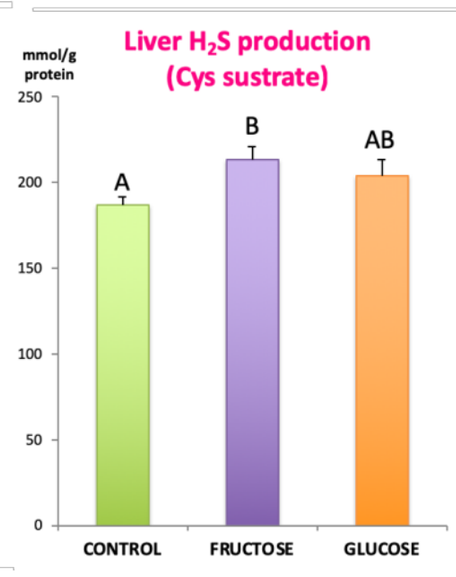






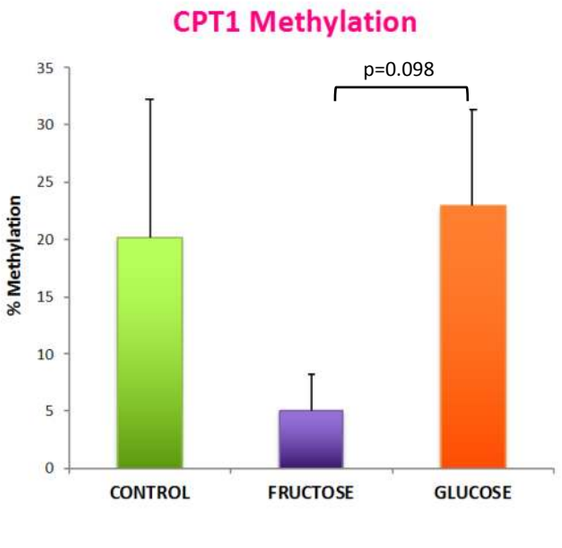


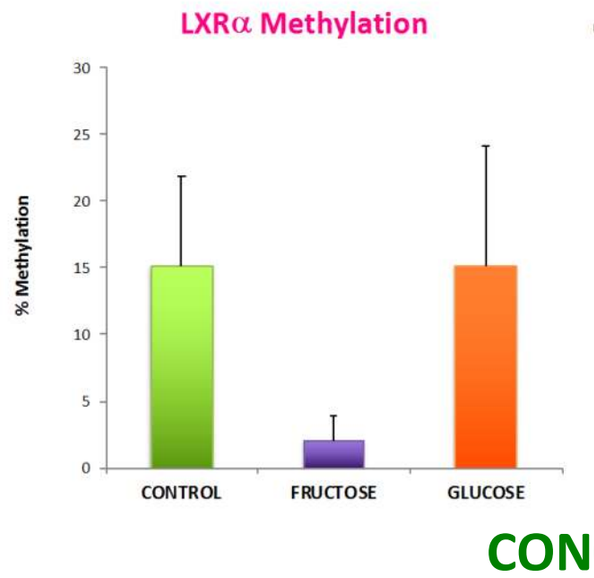


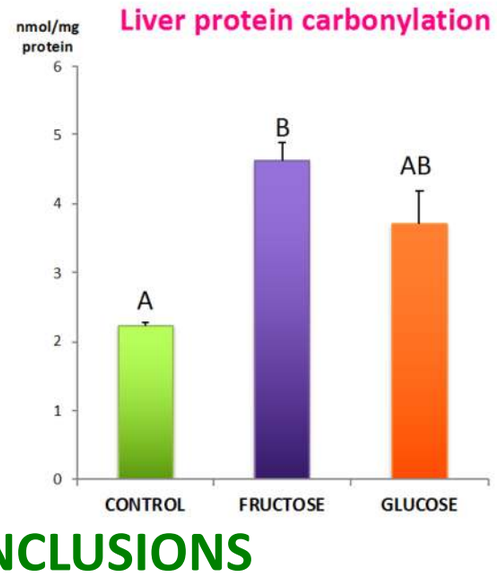


Plasma folic acid is significantly reduced in females from fructose fed mothers. This effect is not related with any of the changes observed in the gene expression of MAT1A (Methionine Adenosyltransferase 1A), MTR (Methionine synthase) and MTHFR (Methyltetrahydrofolate reductase).

Homocysteine (HCy) plasma levels were higher on female descendants of fructose fed mothers compared to the other two groups due to a reduced expression of BHMT (Betaine-Homocysteine-S-Methyltransferase). Surprisingly, CBS (Cystathionine beta-synthase) and CSE (Cystathionine gamma-lyase) showed an opposite profile to BHMT, possibly as a compensatory effect, by converting the excess of HCy to H_2S.







The reduced levels of the methyl-donor folate could lead to an impairment of one-carbon metabolism, affecting both, DNA-methylation and the redox status. Indeed, the promoter methylation of LXRα (Liver X-receptor alfa) and CPT1 (Carnitine Palmitoyltransferase 1) genes was diminished, and protein carbonylation augmented in females from fructose-fed mothers.

CONCLUSIONS

Maternal fructose intake modifies one-carbon metabolism and the transsulfuration pathway in female progeny affecting folic acid and homocysteine plasma levels and, accordingly, the hepatic gene promoter methylation and oxidative stress.

BIBLIOGRAPHY

Rodrigo, S., Fauste, E., de la Cuesta, M., Rodríguez, L., Álvarez-Millán, J. J., Panadero, M. I., Otero, P. & Bocos, C. (2018). Maternal fructose induces gender-dependent changes in both LXRα promoter methylation and cholesterol metabolism in progeny. *The Journal of nutritional biochemistry*, *61*, 163-172.

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