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MATERNAL FRUCTOSE EXPOSURE PROGRAMS METABOLIC SYNDROME-ASSOCIATED BLADDER OVERACTIVITY IN YOUNG ADULT OFFSPRING

Hypothesis / aims of study

Maternal fructose exposure (MFE) programs metabolic syndrome (MetS) in young adult offspring. MetS may have an increased risk of overactivate bladder (OAB) symptoms. Whether MFE programs MetS-associated bladder dysfunction in adult offspring remains unknown.

Study design, materials and methods

Pregnant Sprague-Dawley rats received a fructose-enriched or control diet during pregnancy and lactation. Male offspring were studied for the phenotypes of MetS and voiding behavior at the age of 12 week. Next-generation sequencing and qPCR were used to screen and validate transcript alterations in rat bladders. In vivo cystometry and in vitro detrusor contractility were used to evaluate bladder function. Bladder tissues were obtained for Western blotting of protein expression.

Results

Compared to controls, MFE rat offspring showed bladder overactivity and traits of MetS. Alterations in bladder transcripts, including increased mRNA levels of M_2- and M_3-mAChR, $P2X_1$ receptor, and $VPAC_2$ receptor and decreased mRNA levels of TRPV4 receptor, were found in MFE offspring. Significantly decreased carbachol-induced contractility combined with upregulation of M_2- and M_3-mAChR receptors and $P2X_1$ receptor protein expressions of the bladder were noted in MFE offspring.

Interpretation of results

Results of this study show that MFE during gestation and lactation may induce bladder overactivity and urinary frequency in young adult male offspring. Among the 20 target gene families involved in bladder physiological functions, we identified significant increases in *Chrm2, Chrm3, P2rx1, Vipr2,* and a significant decrease in *Trpv4* mRNA levels. At the same time, the increases in the expressions of M2- and M3-mAChR and $P2X_1$ receptor proteins were noted in the bladder of offspring to the MFE. In bladder functional tests, the MEF offspring showed significantly decreased detrusor contractility induced by high concentrations of carbachol. Taken together, these observations suggest that bladder dysfunction in adult male offspring programmed by MFE is associated with alterations in the bladder transcripts, impairment of the cholinergic pathways of the bladder, and promotion of OAB symptoms.

Concluding message

Our data show that MFE can program MetS-associated bladder overactivity in young adult male rat offspring. Alterations in bladder transcripts, including *Chrm2, Chrm3, P2rx1, Trpv4,* and *Vipr2* gene expression, may be associated with primary or secondary programmed bladder dysfunction in MFE offspring. Decreased carbachol-induced contractility, along with upregulation of M_2- and M_3-muscarinic receptors and $P2X_1$ receptor protein expression in the bladder, may underlie the pathophysiology of programmed bladder dysfunction in adult offspring to MFE.

Disclosures

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