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21797 | Early-life exposure to non-nutritive sweeteners: effects on hepatic FGF21 pathways and mitochondrial function

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Background & Aim: To combat obesity, diets and food products containing non-nutritive sweeteners (NNS), which provide sweetness without caloric intake (1), have gained popularity, even among pregnant women who reported intentional NNS consumption during gestation (2). In 2023, the World Health Organization warned about NNS consumption, as their long-term effects may be associated with an increased risk of type 2 diabetes, cardiovascular diseases, and mortality. Importantly, the environment during early life can induce permanent changes in metabolic health in adult life (3), suggesting that fetal exposure to NNS may induce long-term metabolic dysfunction in offspring (2,4). Fibroblast growth factor 21 (FGF21) is a key regulator of metabolic homeostasis (5). So, this branch of the MHSWEET project aims to study the effects of Rebaudioside A (RebA, the major sweetener component of stevia) exposure during the perigestational period on hepatic lipid metabolism of adult offspring and the involvement of FGF21. **Methods:** Female Sprague-Dawley rats were administered RebA in the drinking water or water as control from 4 weeks before mating until weaning. Food and beverage consumption, morphometric parameters, fasting glucose, oral glucose tolerance, and insulin sensitivity were measured before sacrifice at 10 months of age. Functionality of G1 hepatic mitochondria (OROBOROS® Oxygraph-2k system), hepatic triglyceride levels (Oil-Red-O staining), genes involved in hepatic lipid metabolic pathways and inflammation (RT-PCR) will be evaluated. **Results:** The results obtained so far, showed that RebA exposure increased body weight in adult female offspring and induced dysglycemia in adult male offspring. The remaining studies are still

being conducted. **Conclusion:** Results seem to support the hypothesis that intrauterine exposure to RebA may program offspring to a dysmetabolic state. These results will be useful to improve knowledge, and support public health policies regarding NNS use throughout life.

Keywords: Non-Nutritive Sweeteners, Rebaudioside A, Fetal Programming, Metabolic Dysfunction, FGF21.

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