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Professor Doutor Pedro Rodrigues

jjup@reit.up.pt

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22773 | Early-Life Exposure to Non-Nutritive Sweeteners: Impact on Adipose Tissue Morphology and Metabolic Function

Margarida Oliveira-Barbosa¹; Isabella Bracchi^{2,3}; Elisa Keating²; Rita Negrão²

Department Biomedicine, Unit of Biochemistry, Faculty of Medicine, University of Porto, Porto, Portugal¹; RISE-Health, Department Biomedicine, Unit of Biochemistry, Faculty of Medicine, University of Porto, Porto, Portugal²; Department of Functional Sciences, School of Health, Polytechnic Institute of Porto, Porto, Portugal³

Background & Aim: Non-sugar sweeteners (NSS) are sugar alternatives widely incorporated into food and beverages (1), providing sweetness with negligible caloric contribution (2). Over the past two decades, their consumption has increased among pregnant women (3,4). In 2023, WHO discouraged NSS intake highlighting the need for studies regarding exposure during critical windows of development (5), such as pregnancy and childhood (6). The MHSWEET project explores the role of NSS consumption on fetal programming of metabolic dysfunction. This branch of the MHSWEET aims to evaluate metabolic function of adipose tissue of adult mice exposed *in utero* to Rebaudioside A (RebA), the main sweetener component of the NSS Stevia. It also seeks to determine if this early-life exposure affects offspring's susceptibility to metabolic dysfunction induced by a high-fat diet (HFD). **Methods:** Female Sprague-Dawley rats (G0) ingested RebA in drinking water (4mg steviol eq/kg body weight/day – EFSA's ADI, n=8), or regular water (C, n=8), before mating until weaning (13 weeks). After weaning, offspring (G1) were fed a standard diet (STD) until 8 months of age, when they were administered STD or HFD until 10 months of age, creating 4 groups of study: C/STD, C/HFD, RebA/STD and RebA/HFD. Mesenteric adipose tissue morphology (H&E staining), as well as lipid and mitochondrial metabolic pathways (RT-PCR) will be assessed. **Results:** The results so far showed that RebA exposure increased body weight in female offspring from 30 weeks of age onwards compared to controls (p=0.0165). Blind histological and RT-PCR analyses are ongoing to search for: a) adipocyte hypertrophy potentially induced by RebA exposure or HFD, mainly in RebA exposed offspring and b) alterations in lipid and mitochondrial metabolic pathways that may explain the observed changes in body weight and any changes in adipocyte morphology. **Conclusions:** This study will be crucial to assess health implications of NSS consumption during vulnerable stages of life.

Keywords: Non-Nutritive Sweeteners, Rebaudioside A, Fetal programming, Metabolic dysfunction, Adipose tissue.

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