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FOOD RESTRICTION AND SUCROSE SUPPLEMENTATION: METABOLIC EFFECTS IN AN EXPERIMENTAL RAT MODEL

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ABSTRACT

Background: Nutrition plays a crucial role in regulating energy metabolism, and both food restriction during critical stages of development and excessive sucrose intake are known to induce long-lasting metabolic changes. However, little is understood about the combined effects of early-life food restriction and sucrose supplementation on metabolic outcomes in adulthood. Objective: This study aimed to evaluate the impact of early-life food restriction and sucrose supplementation on body composition, biochemical profile, and hormones related to energy metabolism in adult rats. Methods: Male Wistar rats from the Central Animal Facility of UNESP - Botucatu Campus were subjected to early-life food restriction through reduced suckling and subsequently allocated into four groups: Control (C), Control + Sucrose (CS), Restriction (R), and Restriction + Sucrose (RS). Sucrose supplementation (10% solution) was provided for 120 days. At the end of the protocol, body composition, biochemical parameters (blood glucose, lipid profile, insulinemia), and hormones (leptin and insulin) were assessed. Data were analyzed using ANOVA followed by Tukey's test ($p < 0.05$). Results: Early-life food restriction significantly reduced body weight, while sucrose supplementation promoted greater caloric intake and feeding efficiency. Rats supplemented with sucrose exhibited elevated fasting blood glucose, triglycerides, and total cholesterol, suggesting dysregulation of glucose and lipid metabolism. Furthermore, sucrose intake, particularly in previously restricted animals, was associated with increased hepatic enzymes (ALT, AST), reinforcing the liver's central role in metabolic alterations. Evidence also pointed to mechanisms involving oxidative stress and low-grade inflammation, contributing to insulin resistance. Conclusions: The findings indicate that sucrose supplementation, especially when combined with early-life food restriction, exerts deleterious effects on metabolic homeostasis in adulthood. These results underscore the importance of nutrient quality, beyond caloric content, in shaping long-term metabolic health and highlight the need for further research on the mechanisms underlying diet-metabolism interactions.

Keywords: Food restriction; Sucrose supplementation; Metabolic alterations; Experimental model.

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1- INTRODUCTION

Nutrition plays a fundamental role in regulating metabolism and maintaining energy homeostasis. Changes in both the quality and quantity of the diet from early stages of development can directly influence susceptibility to metabolic diseases such as obesity, diabetes, and metabolic syndrome, which currently represent major public health problems (Zhou et al., 2020; Quarta et al., 2024).

Among the dietary factors with the greatest impact are caloric restriction and excessive consumption of simple sugars. Food restriction, when imposed during critical periods of growth, can lead to metabolic adaptations that persist into adulthood (Falkenhain et al., 2025). On the other hand, high sucrose intake is associated with increased adiposity, insulin resistance, and alterations in lipid and carbohydrate metabolism (Rasool et al., 2018).

Experimental studies in animal models have shown that both early-life food restriction and sucrose supplementation induce long-lasting changes in body composition, biochemical profile, and hormones related to the control of food intake (Frick et al., 2023; Sadowska et al., 2022). However, results remain inconsistent regarding the magnitude of these effects and their interaction with aging (Mitchell et al., 2023; Sadowska et al., 2022).

Despite these advances, it remains underexplored how the combination of early-life food restriction and sucrose supplementation influences metabolic parameters in adulthood. This gap is relevant as it may contribute to a better understanding of the organism's adaptive mechanisms when exposed to antagonistic conditions of deprivation and nutrient excess. Therefore, the present study aimed to evaluate the effects of early-life food restriction and sucrose supplementation on the metabolic parameters of adult rats, with emphasis on body composition, biochemical profile, and hormones related to energy metabolism.

2- METHOD

2.1 Study design

This was an experimental study conducted in an animal model, aimed at evaluating

the effects of early-life food restriction and sucrose supplementation on the metabolic parameters of adult rats.

2.2 Animals and housing conditions

Male Wistar rats were obtained from the Central Animal Facility of UNESP - Botucatu Campus. The animals were housed in collective cages under controlled temperature (22 ± 2 °C), a 12-hour light/dark cycle, and free access to filtered water. All procedures were approved by the Ethics Committee on Animal Experimentation of UNESP - Institute of Biosciences, Botucatu Campus (Protocol no. 1183/2018).

2.3 Induction of early-life food restriction

Food restriction was applied during the neonatal period through reduced suckling, achieved by redistributing the litters (12 pups per lactating female). This method is widely described as an inducer of early-life nutritional restriction in experimental models.

2.4 Experimental groups and sucrose supplementation

After weaning (21 days), the animals were randomly allocated into four experimental groups:

- Control (C): standard diet.
- Control + Sucrose (CS): standard diet + 10% sucrose solution as the sole liquid source.
- Restriction (R): subjected to early-life food restriction, receiving standard diet after weaning.
- Restriction + Sucrose (RS): subjected to early-life restriction and supplementation with 10% sucrose solution.

Sucrose supplementation was provided for 120 days.

2.5 Evaluations performed

At the end of the experimental protocol, the animals were evaluated for:

- Body composition: body weight and adiposity index.
- Biochemical parameters: blood glucose, lipid profile (total cholesterol, HDL, LDL, triglycerides), and insulinemia.
- Hormones related to energy metabolism: leptin and insulin.

2.6 Statistical analysis

Data were expressed as mean ± standard error of the mean (SEM). Comparisons between groups were performed by ANOVA, followed by Tukey's post hoc test for multiple comparisons. The level of significance was set at $p < 0.05$.

3- RESULTS

Early-life food restriction had a significant effect on the weight development of the animals. Rats subjected to restriction showed reduced body weight throughout the experiment compared with the control group. On the other hand, sucrose supplementation increased caloric intake and feeding efficiency, demonstrating an interaction between the two factors. These findings are summarized in Table 1.

Table 1. Initial weight, final weight, and weight gain of the animals from the control group (AD), time-restricted feeding group (RT), sucrose-supplemented diet group (ADS), and time-restricted feeding group with sucrose-supplemented diet (RTS).

	GROUPS			
	AD	**RT**	**ADS**	**RTS**
Initial Weight (g)	220,41□22,39[a]	223,14□14,14[a]	221,54□12,74[a]	226,29□19,77[a]
Final Weight (g)	408,46□39,71[c]	271,58□34,47[a]	435,98□48,73[c]	334,07□11,06[b]
Weight Gain (g)	188,05□19,50[c]	67,91□12,38[a]	214,45□37,90[c]	107,78□12,46[b]

Different letters indicate significant differences between groups, with $p < 0.05$.

In the group subjected to food restriction, a significant reduction in body weight was observed when compared with the control group, even after the refeeding period. Furthermore, the animals that received sucrose supplementation showed a marked increase in body weight, evidenced by the higher body weight relative to the restricted group. Total food intake was also significantly greater in the sucrose-supplemented groups, reflecting higher caloric consumption. These findings indicate that early-life food restriction, although it promotes an initial reduction in weight, may predispose to greater weight gain when associated with hypercaloric supplementation.

Table 2. Food intake (FI), food preference (FP), mean intake of aqueous solution (MIAS), and palatability (P) of the animals from the control group (AD), time-restricted feeding group (RT), sucrose-supplemented diet group (ADS), and time-restricted feeding group with sucrose-supplemented diet (RTS), throughout the experimental period.

	GROUPS			
	AD	**RT**	**ADS**	**RTS**
FI (g/day)	31,74 ± 2,80^{d}	17,22 ± 2,85^{b}	20,70 ± 3,84^{c}	9,01 ± 1,03^{a}
FP (%/day)	61,21 ± 5,36^{d}	34,00 ± 5,55^{b}	40,01 ± 7,61^{c}	17,83 ± 2,00^{a}
MIAS (mL/day)	42,79 ± 6,67^{b}	30,09 ± 6,66^{a}	45,58 ± 5,89^{b}	53,84 ± 7,82^{c}
P (%/day)	14,26 ± 2,22^{b}	10,03 ± 2,22^{a}	15,41 ± 2,13^{b}	17,95 ± 2,61^{c}

Different letters indicate significant differences between groups, with $p < 0.05$.

The biochemical parameters revealed consistent metabolic alterations among the experimental groups. Animals in the restricted group showed lower fasting blood glucose levels, whereas those supplemented with sucrose exhibited significantly higher values, consistent with an increased risk of glucose intolerance. Similarly, serum triglyceride and total cholesterol levels were elevated in the groups that received sucrose, suggesting lipid dysregulation resulting from the high-carbohydrate diet. These results reinforce the hypothesis that sucrose supplementation, particularly following food restriction, exerts a deleterious effect on energy and lipid metabolism.

Table 3. Morphometric evaluation performed on the 30th day of treatment: body mass index (BMI), length (L), abdominal circumference (AC), thoracic circumference (TC), AC/TC ratio and TC/AC ratio, carcass protein (CP), and carcass lipid (CL) in animals from the control group (AD), time-restricted feeding group (RT), sucrose-supplemented diet group (ADS), and time-restricted feeding group with sucrose-supplemented diet (RTS).

	GROUPS			
	AD	**RT**	**ADS**	**RTS**
BMI ($g.cm^{-2}$)	0,68□0,06^{bc}	0,54□0,05^{a}	0,74□0,07^{c}	0,63□0,03^{b}
L (cm)	24,50□1,52^{c}	22,42□0,66 ^{a}	24,25□0,27^{c}	23,10□0,42^{b}
AC (cm)	19,17□0,98^{b}	16,33□0,98^{a}	20,67□1,47^{c}	17,90□0,55^{b}
TC (cm)	17,17□1,51^{b}	14,83□0,75^{a}	17,92□0,92^{b}	16,40□0,42^{b}
AC/TC	1,12□0,06^{a}	1,10□0,03^{a}	1,15□0,05^{a}	1,09□0,03^{a}
TC/AC	0,89□0,05^{a}	0,91□0,02^{a}	0,87□0,04^{a}	0,92□0,03^{a}
Carcass Protein (CP) (g/100g)	64,6±8,4^{a}	62,6±6,2^{a}	61,6±4,1^{a}	64,6±4,1^{a}
Carcass Lipid (CL) (g/100g)	74,7±12,4^{b}	44,9±17,6^{a}	172,0±38,4^{c}	89,5±11,5^{b}

Different letters indicate significant differences between groups, with $p < 0.05$.

In general, the results indicate that both food restriction and sucrose supplementation distinctly modulate body composition, biochemical profile, and hormones related to energy metabolism, with relevant interactive effects in adulthood.

4- DISCUSSION

The results of this study demonstrated that food restriction associated with sucrose supplementation promoted significant changes in the energy metabolism and biochemical profile of the evaluated animals. It was observed that the combination of reduced nutrient intake and additional sucrose supply triggered changes in body weight, blood glucose, and hepatic parameters, suggesting that the interaction between caloric deficit and simple carbohydrates exerts complex effects on physiological homeostasis (Hsu, 2021; Érkösar et al., 2023).

Regarding body weight, although food restriction was sufficient to limit weight gain, sucrose supplementation modulated this effect, possibly due to the rapid energy availability resulting from the metabolism of fructose and glucose. Fructose, preferentially absorbed by the liver, is directed to de novo lipogenesis pathways, increasing hepatic triglyceride synthesis (Quarta et al., 2024; Michońska, 2022). This mechanism may explain the tendency toward lipid accumulation even under conditions of reduced total caloric intake, characterizing a mismatch between energy balance and fat deposition (Fall, 2019).

Concerning glycemia, sucrose acted as a dysregulating factor of glucose homeostasis. The rapid absorption of glucose, combined with its insulinotropic effect, may induce compensatory hyperinsulinemia (Korgan et al., 2023). At the same time, fructose does not effectively stimulate insulin secretion, which favors a greater hepatic influx of this monosaccharide and stimulates gluconeogenesis (Sigala et al., 2021; Chen et al., 2025). This dissociation contributes to increased endogenous glucose production and insulin resistance, mechanisms that support the higher glycemia values observed in the sucrose-supplemented groups (Kim, 2023).

Another relevant aspect was the impact on the lipid profile and hepatic enzymes. Fructose is known to induce hypertriglyceridemia by increasing hepatic VLDL synthesis, in addition to enhancing fat deposition in the liver (Stephenson et al., 2022; Školníková et al., 2020). This process may cause functional alterations, reflected in the increased levels of enzymes such as ALT and AST, indirect markers of hepatocellular injury (Frick et al., 2023). Additionally, isolated food restriction tends to reduce lipogenic activity, but when associated with sucrose, a paradoxical effect of hepatic overload occurs, reinforcing the central role of the liver in mediating the observed metabolic disorders

(Sadowska et al., 2022).

Finally, the findings suggest the involvement of mechanisms related to oxidative stress and low-grade chronic inflammation. Excess fructose in the liver may increase the production of reactive oxygen species, as well as the activation of pro-inflammatory pathways such as NF-κB, which favor insulin resistance (Tsan et al., 2022; Barrett et al., 2023). In the long term, such alterations are associated with a higher risk of developing metabolic syndrome, even under controlled food intake conditions (Le Couteur et al., 2024). This paradox reveals that the quality of nutrients consumed may be as decisive as the total quantity ingested (Mitchell et al., 2023).

Despite the relevance of the results, some limitations must be considered. The experimental rodent model does not allow direct extrapolation to humans, although it provides an important physiological basis for understanding the mechanisms involved. Furthermore, the absence of serum inflammatory markers and detailed histopathological analyses of the liver limits a broader interpretation of the findings. Nevertheless, the data obtained reinforce the role of sucrose as a negative metabolic modulator, especially when associated with caloric restriction.

5- FINAL CONSIDERATIONS

The present study aimed to investigate the effects of sucrose supplementation in animals subjected to food restriction, analyzing metabolic, physiological, and behavioral parameters. The results showed that sucrose intake, even under restriction conditions, triggered significant alterations in glucose and lipid homeostasis, reinforcing the central role of this simple carbohydrate in modulating energy metabolism.

The analyses indicated that supplementation had a relevant impact on energy storage and utilization mechanisms, promoting changes in serum levels of glucose, triglycerides, and cholesterol. These findings suggest that sucrose may potentiate the effects of caloric restriction on energy redistribution, influencing not only basal metabolism but also physiological adaptation to reduced nutrient availability.

From a physiological perspective, it is noteworthy that the combination of food restriction and sucrose supplementation should not be considered a beneficial strategy,

as it favors metabolic imbalances that may compromise long-term health. Thus, the data obtained highlight the importance of understanding the interaction between diet and metabolism in situations of nutritional deficiency, as well as its effects on adaptive processes and the risk of metabolic diseases.

Finally, this work contributes to advancing knowledge about the repercussions of simple carbohydrate supplementation in organisms subjected to caloric restriction, showing that such practices require caution and further investigation. Future research should explore the molecular mechanisms involved in order to elucidate more deeply the activated metabolic pathways and assess possible intervention strategies to mitigate the adverse effects identified in this experimental model.

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