



Intrauterine malnutrition increases O-GlcNAcylation of proteins in neurons and astrocytes in the hypothalamus of young adult offspring.

Poster

Cellular/Molecular, Neurona y glía - Cellular/Molecular, Neurons and glia

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Background: Intrauterine growth restriction (IUGR) is linked to obesity, hypothalamic dysfunction, and impaired glucose metabolism. O-GlcNAcylation, a glucose-dependent post-translational modification, may affect hypothalamic energy balance. This study evaluated O-GlcNAc protein density and colocalization with neuronal (NeuN) and astrocytic (GFAP) markers in the arcuate (ARC), lateral (LH), and ventromedial (VMH) hypothalamic nuclei, as well as food intake and body weight in IUGR animals.

Methods: During gestation, Wistar rats under caloric restriction (**R**) received 50% of control intake (**C**). At 90 days, male pups (n=3/group) were anesthetized, perfused, brains collected, frozen, and sectioned (30 µm). Sections were incubated with primary (anti-O-GlcNAc, anti-NeuN, anti-GFAP) and secondary antibodies (Alexa Fluor 568, 488), and imaged by confocal microscopy. Food intake and body weight were assessed weekly; fluorescence quantified with ImageJ; Student's t-test applied. Study approved by the UNIFESP Ethics Committee (nº1115260121).

Results: R group showed increased O-GlcNAc/GFAP colocalization in ARC and VMH (p<0.001), with reduced astrocytic labeling (p≤0.05). In LH, O-GlcNAc/NeuN

colocalization($p=0.01$) and O-GlcNAc labeling increased($p<0.05$). NeuN labeling decreased in ARC and LH ($p<0.01$). Body weight was lower in R vs C from week 2 post-weaning($p=0.001$), with reduced intake from week 5($p<0.001$), while weight gain remained similar to 90 days.

Conclusion: Overall, IUGR increased neuronal and astrocytic O-glycosylation in key hypothalamic nuclei involved in energy homeostasis, along with reduced neuronal labeling and decreased food intake, while maintaining similar weight gain compared to the control group. These changes suggest altered hypothalamic signaling, with O-GlcNAc as a potential link between IUGR and late-onset obesity.

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