AMYLOID BETA OLIGOMERS INDUCE GLUCOSE METABOLISM DYREGULATION: 
A SUGGESTION OF HYPOTHALAMIC DYSFUNCTION IN ALZHEIMER DISEASE
Da Silva, RAG; Clarke JR; Lyra E Silva NM; Frozza RL; Ferreira, ST; De Felice FG

1Institute of Medical Biochemistry Leopoldo de Meis, Federal University of Rio de Janeiro, Rio de Janeiro, RJ, Brazil. 2School of Pharmacy, Federal University of Rio de Janeiro, Rio de Janeiro, RJ, Brazil.

Alzheimer’s disease (AD) has been increasingly related to metabolic disorders, such as type 2 diabetes (T2D). Epidemiological and clinical data shows that AD patients have impaired glucose metabolism and an increased risk of developing T2D. Amyloid Beta oligomers (AβOs) are toxins that accumulate in AD patient’s brains and are known to inhibit insulin signaling at the hippocampus. In this study, we have the aim to investigate whether AβOs can impact the hypothalamus and also the effects of exercise against AβOs toxicity regarding peripheral metabolic deregulation. To answer those questions, we investigated the impact of 10 pmol of intracerebroventricular (i.c.v.) AβOs injections on hypothalamic levels of proteins related to the insulin signaling pathway, though western blotting. Glucose homeostasis was evaluated through a Glucose Tolerance Test (GTT) which consisted of a dose of 0.5g/kg glucose injection after an overnight fasting period. Exercise training protocol consisted of free swimming 1h/day, 5 days/week for 5 weeks. All the experiments were performed with 8 – 12 weeks old male swiss mice injected with AβOs or Vehicle. Our results show that AβOs can impact the hypothalamus inducing insulin resistance and peripheral glucose intolerance. Moreover, we saw a capability of exercise of preventing the glucose intolerance induced by AβOs i.c.v. injections. These results provide initial information about the impact of AβOs in the hypothalamus and it proposes that physical activity can be a non-pharmacological approach against the impact of AβOs on glucose homeostasis.