Effects of Thyroid Hormone T3 in in cognition, neuroinflammation and apoptosis in an Experimental Model of Alzheimer's disease.

Introduction: Alzheimer's disease (AD), a chronic neurodegenerative disease, is the most common form of dementia. One of its main clinical symptoms is the inability to form recent memories. However, with the disease progression, a decline in cognitive scale is installed, leading to social dependence and premature death. The exact pathological mechanisms of AD are still misunderstood. Studies suggest that disturbances in glucose metabolism and brain insulin signaling are associated with AD progression and cognitive deficit. In this sense, thyroid hormones (THs) are essential for the maintenance of metabolism and an ideal cognitive state in aging, promoting neurogenesis, myelination, and cell repair. Therefore, the literature suggests that THs can modulate insulin signaling and that their lack or excess are involved with neurological symptoms. Thus, the aim of this study is to evaluate the effects of effects of triiodothyronine (T3) thyroid hormone supplementation in cognitive performance related to animals' memory, neuroinflammation and apoptosis.

Method: Males wistar rats weighing 300- 350 g (n=7-8), received bilateral injections (totaling 4 µL) of vehicle or streptozotocin (2 mg / Kg; Sigma) in the lateral ventricle by stereotaxic surgery to induce AD model. The animals that received the vehicle and STZ were supplemented with a daily intraperitoneal supra-physiological dose of 1.5 µg / 100g of triiodothyronine (T3) or the same volume of vehicle (saline), from the day of stereotaxic surgery, for 30 days. Neuroinflammation and apoptosis were assessed by Western Blot. The animals were also evaluated for motor activity, and cognitive memory performance in novel Object Recognition Behavioral Test. All the experiments were approved by animal ethical committee (CEUA) (protocol nº 023/2016).

Results: The data analysis revealed that T3 supplementation promotes improvement in cognition in the object recognition index of the short and long-term tests ($p < 0.01$), a reduction in GFAP levels by 33% ($p = 0.0326$) and decreased by 36% the pro-apoptotic stimulus given by the relationship between BCL2 and BAX proteins ($p = 0.0380$) after treatment with T3 in animals with AD.

Conclusion: Our data provide evidence of the positive effects of T3 supplementation in relation to cognition and neuroinflammation in a model of AD. Thus, this work highlighting the importance of this therapy and identify mechanisms of action that can be useful on the establishment of therapeutic strategies.