**Thyroid hormone signaling in mouse brain following Pilocarpine-induced status epilepticus**

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**Introduction:** Thyroid hormones (TH) play an important role in the maintenance of central nervous system (CNS) through the control of gene expression [1,2]. Thyroid gland synthesize about 93% of T4 and 7% of T3, the active form of TH [3]. The activation of T4 to T3 in the brain is catalyzed by type 2 iodothyronine deiodinase (D2). Although serum concentration of THs is remarkably stable, D2 regulate T3 signaling in the neurons in a precise spatio- and temporal-manner by controlling the activation of TH [4,5]. D2 expression and activity can change in critically ill patients and consequently the T3 signaling in the tissues [6]. Status epilepticus (SE)is a well-known insult to the CNS that can be defined as a state of continuous seizure activity or two or more sequential seizures without full recovery of consciousness between seizures and may leads to the development of Temporal Lobe Epilepsy (TLE) [7]. Here we hypothesize that seizures could induce changes in D2 expression and activity in the brain with consequent variations in T3 signaling. The shift in T3 signaling could be involved in the altered behavior observed in patients with TLE. Thus, we studied prefrontal cortex, amygdala and hippocampus of mice after induction of SE to evaluate expression and activity of D2 and mRNA levels of T3 regulated genes.

**Methods:** 2 months old C57Bl/J6 male mice were treated with lithium-pilocarpine as a model of epilepsy [8,9]. The seizures were interrupted by Diazepam 3 hours after the beginning of SE and the mice were killed 30 minutes after that. mRNA levels of D2 and T3-regulated genes were analyzed by real-time PCR, and we also analyzed the enzymatic activity of D2.

**Results:** Notably, SE caused an increase in D2 mRNA levels and its activity in the hippocampus, amygdala and prefrontal cortex. mRNA levels for 4 negative regulated genes (Hapln1, Dgkg, Fxyd6, Syce2) decreased and 1 (Slc1a3) increased, and 1 positive regulated gene (Itga7) decreased in hippocampus; 3 negative regulated genes (Hapln1, Dgkg, Slc1a3) decreased and 2 positive regulated genes (Rc3, Aldh1a1) decreased in prefrontal cortex; 1 negative regulated gene (Fxyd6) decreased and 1 positive regulated gene (Aldh1a1) decreased in amygdala.

**Discussion:** Our data showed changes in TH signaling in mice brain after SE. These changes are possibly due to the increase in D2 expression and activity, although we cannot conclude that this resulted in a hyperthyroid brain since there is a significant variation in the expression of T3 regulated genes.

**Conclusion:** Our results showed that SE causes subtle changes in some T3-regulated genes suggesting changes in T3 signaling in the brain.

**References:** [1] Bernal J., Vitam Horm 71:95-122, 2005; [2] Hernandez A et al., Endocrinology 153(6):2919-2928, 2012; [3] Larsen PR et al., William’s Textbook of Endocrinology 10ª ed:331-373, 2003; [4] Gereben B et al., Cell Mol Life Sci 65(4):570-590, 2008; [5] Dentice M et al., Biochim Biophys Acta 1830(7):3937-45, 2013; [6] Bianco AC et al., The Journal of Clinical Investigation 116(10):2571-2579, 2006; [7] Lowenstein DH et al., Epilepsia 40(1):120-2, 1999; [8] Curia G et al., J Neuroscience Methods 172:143-157, 2008; [9] Levésque M et al., J Neuroscience Methods 260(15): 45-52, 2015.