Reverse T₃ Alters the Oxidative Stress Induced by Congenital Hypothyroidism in Hippocampus of Immature Rats

Domingues, J.T.¹,²; Almeida, B.A.N.¹; Cattani, D.¹,²; Parisotto, E.B. ²,³; Wilhelm Filho, D³; Silva, F.R.M.B.¹, Zamoner, A.¹

¹Departamento de Bioquímica, CCB, UFSC, Florianópolis, SC; ²Programa de Pós-Graduação em Farmácia, UFSC, Florianópolis, SC, Brazil; ³Departamento de Ecologia e Zoologia, CCB, UFSC, Florianópolis, SC, Brazil.

Congenital hypothyroidism leads to hypomyelination, oxidative damage and mental retardation. The aim of this study was to investigate the nongenomic effects of reverse T₃ (rT₃) on the hypothyroid-induced oxidative stress in hippocampus of immature rats. Congenital hypothyroidism was induced in rat dams by adding 0.05 % 6-propyl-2-thiouracil in the drinking water during gestation and suckling period. Experiments were carried out with 15 day-old pups. Hippocampal slices from control and hypothyroid pups were pre-incubated in Krebs-Ringer bicarbonate (KRb) for 15 min and then incubated with or without rT₃ 10⁻¹⁰ M during 30 min. In order to investigate the involvement of extracellular-regulated kinase 1/2 (ERK1/2) in the mechanism of action of rT₃, PD98059 was added during pre-incubation and incubation periods. Then, we determined the levels of GSH and TBARS, as well as the enzymatic activities of glucose-6-phosphate dehydrogenase (G6PD), gamma-glutamyl transferase (GGT) and catalase in hippocampal slices of hypothyroid young rats treated with rT₃. Results revealed that rT₃ reversed the lipid peroxidation induced by hypothyroidism in rat hippocampus. Moreover, rT₃ restored the depletion in GSH levels caused by the hypothyroid condition. Furthermore, hypothyroidism inhibits G6PD and GGT activities in rat hippocampus and these effects were also reversed by rT₃. However, catalase activity was unaltered by the hormonal treatment. Our results demonstrated that short-term exposure (30 min) to rT₃ (commonly referred as an inactive metabolite of thyroid hormones) might modulate the compromised antioxidant defense system in hypothyroid rat hippocampus. In addition, the mechanism of action of rT₃ is dependent on ERK1/2 activation. Taken together, our data showed a nongenomic effect of rT₃ which may protect the brain for the oxidative damage induced by congenital hypothyroidism.

Word Keys: hypothyroidism, hippocampus, reverse T₃, oxidative stress.

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