Effect of Reverse T_{3} on Hypothyroid-Induced Oxidative Stress in Immature Rat Hippocampus

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INTRODUCTION: Thyroid hormones are critical factors controlling development and function of central nervous system. Congenital hypothyroidism is associated with hypomyelination, oxidative damage and mental retardation. The aim of this study was to investigate the nongenomic effects of reverse T\(_{3}\) (rT\(_{3}\)) on the hypothyroid-induced oxidative stress in hippocampus of immature rats. METHODS: Congenital hypothyroidism was induced in Wistar rat dams by adding 0.05 % 6-propyl-2-thiouracil in the drinking water during gestation and suckling period (experimental protocol approved by the ethical committee CEUA/UFSC#PP00820). Hippocampal slices from 15 day-old euthyroid (E) and hypothyroid (H) pups were pre-incubated in Krebs-Ringer bicarbonate (KRb) for 15 min and then incubated with or without rT\(_{3}\) \(10^{-9}\) M during 30 min. In order to investigate the CaMKII and PKA in the mechanism of action of rT\(_{3}\), KN93 or H89, respectively, was added during pre-incubation and incubation periods. Then, the GSH and TBARS levels were determined, as well as the enzymatic activities of glucose-6-phosphate dehydrogenase (G6PD), gamma-glutamyl transferase (GGT) and catalase were measured in hippocampal slices of hypothyroid young rats treated with rT\(_{3}\).

RESULTS AND DISCUSSION: Results revealed that lipid peroxidation induced by hypothyroidism in rat hippocampus might be reversed by short-term exposure to rT\(_{3}\) (E= 431.3 ± 34.2 nmol/g; H= 625.5 ± 73.0 nmol/g; H+rT\(_{3}\)= 467.6 ± 40.9 nmol/g; N=8). Moreover, rT\(_{3}\) restored the depletion in GSH levels caused by the hypothyroid condition (E= 1.07 ± 0.074 mmol; H= 0.60 ± 0.02 mmol; H+rT\(_{3}\)= 0.78 ± 0.03 mmol; N=8). Furthermore, hypothyroidism inhibits G6PD (E= 1.8 ± 0.12 U/μg protein; H= 1.25 ± 0.05 U/μg protein; H+rT\(_{3}\)= 1.96 ± 0.01 U/μg protein; N=8) and GGT (E= 2.06 ± 0.18 U/μg protein; H= 1.33 ± 0.05 U/μg protein; H+rT\(_{3}\)= 1.98 ± 0.19 U/μg protein; N=8) activities in rat hippocampus and these effects were also reversed by rT\(_{3}\). However, catalase activity was unaltered by the hormonal treatment. Our results demonstrated that short-term exposure (30 min) to rT\(_{3}\) (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 rT\(_{3}\) in modulating GGT activity is dependent on PKA (H= 1.35 ± 0.01 U/μg protein; H+rT\(_{3}\)= 2.03 ± 0.05 U/μg protein; H+rT\(_{3}\)+H89= 1.19 ± 0.2 U/μg protein; N= 8) and CaMKII (= 1.25 ± 0.01 U/μg protein; H+rT\(_{3}\)+KN93= 2.13 ± 0.12 U/μg protein; H+rT\(_{3}\)+KN93= 1.03 ± 0.01 U/μg protein; N=8) activation. CONCLUSION: Taken together, our data showed a nongenomic effect of rT\(_{3}\) which may protect the brain for the oxidative damage induced by congenital hypothyroidism.

Word Keys: hypothyroidism, hippocampus, reverse T\(_{3}\), oxidative stress.

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