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OXIDATIVE DAMAGE IN BRAIN OF DIABETIC RATS SUBMITTED TO FORCED SWIMMING TEST: THE INSULIN AND CLONAZEPAM EFFECT

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Introduction: Diabetes Mellitus (DM) is considered one of the major metabolic diseases of 21st century. DM is a hyperglycemic chronic state that may modify central nervous system functions and is associated with moderate cognitive deficits and neurophysiological and structural changes in the brain, a condition that may be referred to as diabetic encephalopathy^{1,2}. Psychiatric manifestations seem to accompany this encephalopathy, since the prevalence of depression in diabetic patients is much higher than in the general population, and clonazepam is being used to treat this complication². It is known that there is oxidative stress in peripheral blood in experimental animal model of diabetes and depression, and acute treatment with insulin and clonazepam has a protective effect on oxidative stress in this model.

Objective: the objective of this study is evaluate the effect of insulin and/or clonazepam on oxidative stress parameters in brain areas (cortex, hippocampus and striatum) of diabetic male rats induced with streptozotocin and submitted to forced swimming test (FST).

Materials and Methods: diabetes will be induced by a single i.p. dose of STZ 60 mg/kg in male *wistar* rats. Insulin acute i.p. treatment (4 IU/kg) and/or CNZ acute i.p. treatment (0,25 mg/kg) will be administered 24, 5 and 1 hour before the FST. Nondiabetic control rats will receive i.p. injections of saline (1 ml/kg)³. Animals will be sacrificed by decapitation and brain areas will be collected. The protein oxidative damage will be evaluated by carbonyl formation⁴ and by total thiol groups⁵; the lipid peroxidation will be measured by malondialdehyde (MDA) levels⁶; the antioxidant status will be analysed by total antioxidant potential (TRAP)⁷, total antioxidant reactivity (TAR)⁷ and by the analyses of enzymatic activities (superoxide dismutase, catalase⁸ and glutathione peroxidase); the DNA damage will be determined by comet assay⁹. The biochemical markers glycemia and insulin levels will be determined. Therefore, we aimed to check the central effect of clonazepam and insulin on oxidative stress in an animal model of diabetes and depression, and try to elucidate the mechanisms involved in diabetic encephalopathy.

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