PGE1 DELIVERED BY LIPOSOMES ANTAGONIZED DENDRITIC SPINE LOSS AND REDUCTION OF VEGF AND VEGF-R2 IN FRONTAL CORTEX AND HIPPOCAMPUS OF DIABETIC RATS

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Diabetes (type 1 and 2) is a common metabolic disorder that can lead to functional and structural neurological complications such as cognitive impairment, dementia and reduced volume of hippocampus and frontal cortex. Diabetes related impairments in cognition and neural structure and function could be the consequence of a progressive damage at vascular level. Given that prostaglandins (cyclic oxygenated fatty acids) exert a potent positive action on vascular endothelium in many tissues, we used one of these molecules (PGE1) to prevent or ameliorate the negative effects of diabetes in vascular district in a rat model of diabetes (streptozocin treated rats). Since prostaglandins are rapidly metabolized by different enzimes we included PGE1 into liposomes made with phosphatidilcholine and Poly-L-lysine. These liposomes (1µg/kg) were intraperitoneally administered (twice a week for three months) to streptozotocin (70 mg/Kg) treated rats. Healthy control rats and diabetics rats treated with saline have been used as control; all rats were sacrificed after three months. The glycemia was checked one time a week and 1 UI insulin retard administered once a week. In diabetes rats the dendritic spines density, VEGF (vascular endothelial growth factor) and VEGF-R2 (tyrosine kinase receptor of VEGF) expression levels were markedly reduced in the hippocampus and frontal cortex. As expected, the morphology and some molecular parameters of gastrocnemius muscle, lungs and kidneys showed a dramatic alteration effects almost completely reversed by PGE1 treatment. The results suggest that PGE1 treatment has great efficacy in antagonizing the neurochemical and molecular consequences elicited by experimental diabetes both in brain and periphery. The reduced expression of dendritic spines densities, associated to the impairment of learning and memory present in this pathology, are consistent with the structural brain damage and functional decline present in diabetes patients.