Mitochondrial Parameters in Proliferative and Differentiated Human Neuroblastoma Cell Line SH-SY5Y Challenged with 6-hydroxydopamine

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Mitochondrial dysfunction and oxidative stress have been strongly related to the pathogenesis of Parkinson disease (PD). However, the molecular mechanisms leading to dopaminergic neuron death are not well known. Even though proliferative human neuroblastoma cell line SH-SY5Y is widely used as experimental model for PD studies, differentiated cells possibly represent a more suitable model. Here we evaluated the differences between proliferative and differentiated SH-SY5Y cells in a model of PD induced by 6-hydroxydopamine (6-OHDA), focusing mainly in the mitochondrial dysfunction. Ten days of treatment with retinoic acid (10 µM) in medium (DMEM/F12) plus 1% FBS induces morphological (presence of neurite-bearing cells) and biochemical (expression of tyrosine hydroxylase) changes in SH-SY5Y cells. 6-OHDA citotoxicity was determined by MTT assay in both cellular models. Drug GI_{50} varied two-fold higher in proliferative cells compared to differentiated cells. As an index of mitochondrial dysfunction caused by 6-OHDA treatment, we performed a time course experiment to determine the loss of mitochondrial membrane potential, using the JC-1 fluorescence dye. Once initiated the depolarization, mitochondrial fraction were isolated and a proteomic and redox-proteomic analysis were performed. Our data demonstrated that both cell lines have different sensitivities to 6-OHDA that could be related in part with the differences in the pattern of protein composition and oxidative targets in mitochondria. Our findings support the use of human neuron-like cells (differentiated) instead of human neuroblastoma cells line as a better experimental model to elucidate the molecular mechanism related to the pathogenesis of PD.

Key words: *6-hydroxydopamine, mitochondria, Parkinson disease*

Supported by: CNPq