DOPAMINE AND L-DOPA INCREASE *IN VITRO* PROLIFERATION OF STEM CELLS FROM THE MOUSE SUBVENTRICULAR ZONE

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The subventricular zone (SVZ) in mammalian brain contains neural stem cells that have the potential to produce new neurons, astrocytes and oligodentrocytes. Since dopaminergic nigrostriatal projections regulate neural precursor proliferation in the adult mouse SVZ(1), we deemed of interest the study of both dopamine (DA) and its precursor L-DOPA effects on in vitro proliferation of stem cells from the mouse SVZ. We used neurosphere-derived stem cells that were established from the periventricular region of the forebrain ventricles of adult C57BL/6 mice (2). Cell viability was assessed by MTT assay. Results. Both DA and L-DOPA (10-25 and 50 μM, incubation time 24h) showed a concentration-related increase in stem cell proliferation. In fact, DA or L-DOPA 50 μM increased cell viability by 74 and 97%, respectively. When associated, DA and L-DOPA showed an additive synergism (+174% at the higher concentration). Both DA and L-DOPA, which as catechol-containing compounds undergo autoxidation, are known to induce apoptotic cell death in culture of several cell lines. Moreover, manganese (Mn) is know to increase L-DOPA autoxidation in vitro as well as in vivo (3), with a consequent increase in L-DOPA cytotoxicity. We deemed of interest, therefore, the evaluation of low Mn concentrations on L-DOPA effects on stem cell viability. Mn alone (25 and 200 μM, incubation time 24 h) decreased stem cell viability by about 22 and 60%, respectively. When L-DOPA 50 μM was added, cell viability further decreased (by about 46 and 84%, respectively). Ascorbic acid (AA) 100 μM induced a significant recovery in cell viability in both experiments. Conclusions. The results of this study demonstrate that both DA and L-DOPA stimulate neurosphere-derived stem cells proliferation. In turn, neurosphere-derived stem cells protect both DA and L-DOPA from autoxidation. These data may be of relevance to the use of neurosphere-derived stem cells to afford neuroprotection in animal models of PD. However, the Mn-induced switch of L-DOPA effect from increase in proliferation to decrease in cell viability, and the protective effect of AA, outline the fundamental role of the antioxidant system of the extracellular compartment.

1 Baker S.A.,Baker K.A. and Hagg T. J.Neurosci.,20: 575-579, 2004. **2** Pluchino S., Zanotti L., Rossi B., Brambilla E., Ottoboni L., Salani G., Martinello M., Cattalini A., Bergamini A., Furlan R., Comi G., Constantin G. and Martino G. Nature, 436: 266-271, 2005. **3** Serra P.A., Esposito G., Enrico P., Mura M.A., Migheli R., Delogu M.R., Miele M., Desole M.S., Grella G., and Miele E. Br.J.Pharmacol.,130: 937-945, 2000.