

COMBINED ADMINISTRATION OF AN A_{2A} RECEPTOR ANTAGONIST AND A 5-HT_{1A/1B} RECEPTOR AGONIST REVERSES NEUROINFLAMMATION IN THE 6-OHDA MODEL OF PARKINSON'S DISEASE

Giulia Costa¹, Marcello Serra¹, Micaela Morelli¹, Annalisa Pinna²

¹Department of Biomedical Sciences, Section of Neuropsychopharmacology, University of Cagliari, Cagliari - Italy, ²National Research Council of Italy, Institute of Neuroscience, Cagliari - Italy

Introduction: A previous study of our laboratory demonstrated an improved motor performance in 6-hydroxydopamine (6-OHDA) unilaterally lesioned rats, a model of Parkinson's disease (PD), that were treated with the combination of L-dopa, the serotonin 5-HT_{1A/1B} receptor agonist eltoprazine, and the adenosine A_{2A} receptor antagonist preladenant. Starting from these findings, and from evidences that implicates neuroinflammation in PD progression, the present study investigated whether counteraction of neuroinflammation participated in the motor effects of the L-dopa+eltoprazine+preladenant combination.

Materials and methods: 6-OHDA-lesioned rats were chronically treated with L-dopa+eltoprazine+preladenant. Then, we evaluated in the denervated caudate-putamen (CPu) and substantia nigra pars compacta (SNc) the immunoreactivity (IR) for the glial fibrillary acidic protein (GFAP), and the co-localization of the ionized calcium binding adaptor molecule 1 (IBA1), with interleukin (IL)-1 β , tumor necrosis factor- α (TNF- α) and IL-10. Finally, the IR for tyrosine hydroxylase (TH) and the dopamine (DA) transporter (DAT) was quantified.

Results: Combined treatment with L-dopa+eltoprazine+preladenant induced a reduction of basal GFAP and IBA1IR in both CPu and SNc. Moreover, a reduction of IL-1 β in IBA1-positive cells both in CPu and SNc and of TNF- α in IBA1-positive cells in SNc was observed. Besides, a significant increase in IL-10 in IBA1-positive cells was also observed in SNc. Finally, a significant reduction of DAT and TH IRs was found in all the experimental groups.

Discussion and conclusions: The present findings indicate that the combined administration of L-dopa + eltoprazine + preladenant reduced the inflammatory and neurodegenerative responses in the nigrostriatal system of 6-OHDA-lesioned rats.