PROTECTIVE EFFECT OF THE MAO-B INHIBITOR PF9601N IN A MICRODIALYSIS MODEL OF EXCITOTOXICITY

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Introduction: Parkinson's disease (PD) is characterised by a progressive loss of the nigrostriatal dopaminergic neurons, leading to a severe depletion of dopamine in the substantia nigra and striatum. PF9601N [N-(2-propynyl)-2-(5-benzyloxy-indolyl) methylamine], an acetylenic triptamine derivative, is a MAO-B inhibitor more potent and selective than l-deprenyl that showed neuroprotective properties in several in vitro and in vivo models of PD.

Aim: To evaluate the effect of PF9601N against excitotoxicity which is also involved in the pathophysiology of PD.

Methods: Excitotoxic insult was induced by the local administration of kainate (KA) in the striatum of freely-moving adult rats by microdialysis. We evaluated the release of amino acids and amines by HPLC and we also performed a histological study 48h-after KA administration.

Results: We observed that PF9601N is able to reduce the KA-evoked release of the excitatory neurotransmitters glutamate and aspartate and to increase the output of the inhibitory and neuroprotective amino acid, taurine. Nevertheless, it did not produce any effect on the release of dopamine and its metabolites, HVA and DOPAC as well as 5HIAA, the main metabolite of serotonin, which could not be evaluated from the perfusate samples in our experimental conditions. Moreover, it prevented glial activation and reduced the percentage of apoptotic nuclei induced by KA.

Conclusion: We can conclude that the neuroprotective effects observed by PF 9601N were exerted by itself and that its metabolite does not play any role in the beneficial properties of this compound in this in vivo model of excitotoxicity.