THE INFLUENCE OF ACUTE AND PROLONGED INFLAMMATION ON PARAQUAT TOXICITY AND THE EXPRESSION OF α-SYNUCLEIN AND SYNPHILIN-1 IN THE NIGROSTRIATAL PATHWAY IN RATS

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Introduction: Prolonged inflammation, oxidative stress and protein aggregation are the factors contributing to the Parkinson's disease (PD) pathology. The pesticide paraquat (PQ) is an environmental substance increasing incidence of PD and has been used to model this disease.

Aims: We examined if acute or prolonged inflammation would aggravate PQ toxicity in the nigrostriatal dopaminergic pathway or change the expression of α-synuclein and synphilin-1.

Methods: LPS (10 µg/kg, ip) was administered either once, 3 hours before the first of 4 weekly doses of PQ (10 mg/kg, ip) or 4 times, before each of PQ doses. Animals were killed 7 days after the last dose of PQ. The body temperature was measured. HPLC-EC analysis of DA and its metabolites was performed in the striatal homogenates. The density of dopaminergic cells (TH+) was calculated stereologically in the substantia nigra (SN). The expression of α-synuclein and synphilin-1 and active microglia marker CD11b was measured in SN.

Results: A single LPS pre-treatment aggravated PQ toxicity in SN. Neurodegeneration of dopaminergic neurons was also observed after prolonged inflammation. Interestingly repeated LPS administration combined with PQ did not enhance this effect. PQ decreased the body temperature and microglia activation in SN while LPS showed the opposite effect. Repeated LPS decreased the expression of α-synuclein while only the combined treatment lowered the levels of synphilin-1 in the SN.

Conclusions: PQ and LPS act through counteracting mechanisms probably on the microglia activation.

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