EFFECTS OF SYSTEMIC MPTP ADMINISTRATION ON BEHAVIOR AND DOPAMINE CHANGES IN DIALYSATE FROM THE STRIATUM OF FREELY MOVING MICE

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The neurotoxin MPTP represents a reliable animal model of Parkinson's disease (PD). We investigated, in groups of 5 C57BL/6 freely moving mice, whether MPTP-induced behavioral changes might be correlated with changes in striatal dialysate dopamine (DA) concentrations. Open field, ethogram, grid and swimming tests were performed during administration of MPTP 25 mg/kg i.p. daily dose for 5 consecutive days and 7 days after MPTP discontinuance. Dialysate DA concentrations after the 1st, the 5th MPTP dose and 7 days after MPTP discontinuance were quantified by HPLC. Behavioral scores were recorded at the same time points by means of a video camera connected with a PC. Data were quantified using a custom made locomotor activity software.Results. The 1st MPTP dose induced a long-lasting increase in dialysate DA with a peak of 19.1±3.2 nM (8 times baseline) after 100 min. At the end of MPTP treatment (day 5th), baseline dialysate levels if DA were significantly reduced by about 90%, compared to controls. MPTP administration induced a short-lasting increase in dialysate DA, with a peak of 3.72±1.12 nM after 40 min. Seven days after MPTP discontinuance, baseline dialysate DA showed a significant trend to recovery. Moreover, MPTP administration induced a long-lasting increase in dialysate DA, with a peak of 9.3±1.4 nM after 60 min. Soon after the first MPTP administration, i) the open field test showed a decrease in locomotor activity; ii) the ethogran showed tremor, freezing and freezing tail; iii) the grid test showed a significant score increase in contact wall, forepaw faults, and a decrease in step distance; iv) the swimming test showed a great score decrease, as compared to controls. At the end of MPTP treatment (day 5th), all the behavioral tests showed a greater impairment. Seven days after MPTP discontinuance, open field and ethogram tests showed a complete recovery, while grid and swimming tests still showed impairment of various degree. Conclusions. Besides the impairment of the nigro-striatal dopaminergic functioning, MPTP proved to be a reliable tool for the in vivo evaluation of extracellular striatal DA concentrations. Following the 1st MPTP systemic administration, behavioral changes appeared to be unrelated to the extracellular striatal DA concentrations. At the end of MPTP treatment and 7 days after its discontinuance, changes in some tests well correlated with extracellular DA. The lack of complete recovery of both grid and swimming tests indicates these latter as reliable tests for the in vivo assessment of the efficacy of therapeutic approaches in the MPTP model of PD.