EARLY DIAGNOSIS OF PARKINSON`S DISEASE VIA PROVOCATION TEST WITHOUT PERIPHERAL NOREPINEPHRINE DEPLETION

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Aims
Developing early (preclinical) diagnosis of Parkinson's disease (PD) remains ongoing issue. Previously we have shown that α-methyl-p-tyrosine (αMPT), a reversible inhibitor of dopamine synthesis, could be used as provocation diagnostic test in MPTP-treated mice model of preclinical PD. This test is based on a reversible enhancement of the dysfunction of degrading nigrostriatal dopaminergic system to a threshold where motor symptoms appear. However, systemic administration of αMPT also affects peripheral dopamine and norepinephrine synthesis, leading to an increased risk of side effects in clinical practice. To overcome this issue, we suggest a combination of αMPT with droxidopa (L-DOPS), synthetic precursor of norepinephrine.

Methods
Catecholamines in brain structures and internal organs of normal and MPTP-treated mice model of preclinical PD were evaluated via HPLC with electrochemical detection. Mice motor activity was assessed with open-field test.

Results
Combination of 200 mg/kg αMPT and 50 mg/kg L-DOPS reduced dopamine but didn't affect norepinephrine concentration in all analyzed brain structures and peripheral organs both in normal and MPTP-treated mice. Moreover, motor behavior was impaired only in MPTP-treated mice 5 hours following αMPT+L-DOPS treatment with the selected doses.

Conclusions
Thus, we improved αMPT-based provocation test for further clinical application by combining it with L-DOPS administration to protect the peripheral norepinephrine synthesis.

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