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MEETING ABSTRACT

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Effects of hemantane on the activity of proline-specific endopeptidases in plasma of rats with experimental Parkinson's disease

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Background: Proline-specific endopeptidases—DPP-4 (dipeptidyl peptidase 4; EC 3.4.14.5) and PEP (prolyl endopeptidase; EC 3.4.21.26)—and the peptides that they hydrolyse are involved in the pathogenesis of neurodegenerative diseases such as Parkinson's disease (PD), Alzheimer's disease and others. The aim of this study was to evaluate the levels of activity of DPP-4 and PEP in two models of experimental PD and assess the effects of hemantane (*N*-2-(adamantyl)-hexamethylenimine hydrochloride), a novel antiparkinsonian drug with potential neuroprotective activity, which was developed in the Zakusov Institute of Pharmacology.

Methods: PD was induced in rats by rotenone (2.75 mg/kg per day for 7 days, i.p.) and by injection of 6-hydroxydopamine (6-OHDA; 12 µg) into the left medial forebrain bundle (MFB). Blood plasma was taken on day 20 after the first rotenone injection and on day 35 after injection of 6-OHDA. Hemantane (10 mg/kg) was administered 10 min prior to rotenone during 7 days, or during 21 days daily starting from day 14 after injection of 6-OHDA. Detection of DPP-4 and PEP activity was carried out by fluorometric assay.

Results: In rats with rotenone-induced PD, a 44.3% increase of PEP activity was determined compared to intact animals ($p < 0.05$). Hemantane caused a 29.7% decrease of PEP activity compared to non-treated rats ($p < 0.05$). DPP-4 activity in this model of PD did not change; hemantane also had no effect on DPP-4 activity compared to non-treated animals. In rats with 6-OHDA-induced PD no changes in PEP activity were revealed as well as no effect of hemantane. In rats with 6-OHDA-induced PD a 17.2% increase of DPP-4 activity compared to sham-operated animals ($p < 0.05$) was determined. In rats which were treated with hemantane, a further increase of DPP-4 activity (by 18% compared to non-treated rats, $p < 0.05$) was found.

Discussion: PEP is known to promote α-synuclein aggregation. The rotenone model of PD is the only model where altered α-synuclein accumulation was reproduced. The ability of hemantane to reduce PEP levels suggests that the drug could possess PEP inhibitory properties. The PD model using 6-OHDA administration into the MFB is a model of more severe PD. In this model hemantane failed to decrease motor disturbances in previous studies as well as DPP-4 activity in the current assay.

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