

Effects of intrastriatal memantine infusion in a mouse model of hemiparkinsonism

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Parkinson's disease is a neurodegenerative disorder caused by loss of nigrostriatal dopaminergic neurons. For over 40 years, levodopa had been established as a gold standard for PD treatment. However, long-term treatment with levodopa is often complicated by the development of adverse effects such as abnormal involuntary movements (AIMs), referred to as levodopa-induced dyskinesia (LIDs). We here report the pharmacological effects of the intrastriatal infusion of memantine, a non-competitive *N*-methyl-D-aspartate (NMDA) receptor antagonist, in a 6-OHDA-lesioned mouse model of hemiparkinsonism. Spontaneous and apomorphine-induced rotational activities with an abnormal hind limb stepping were assessed as Parkinsonian symptoms. Daily intraperitoneal injection of levodopa (15 mg/kg) was performed for 21 days, with assessing AIMs score as an index of LID development. Intrastriatal memantine infusion targeted into the right dorsal striatum, using an iPRECIOTM programmable micro infusion pump with a brain infusion kit, was examined with 4 doses (3 days/dose). Infusion of memantine significantly alleviated Parkinsonian symptoms, and it also reduced AIMs score with a dose-dependent manner. These results support the idea that over-activation of the striatal NMDA receptor function might generate both Parkinsonian symptoms and LIDs.