Contribution of the mGluR7 receptor to antiparkinsonian-like effects in rats: a behavioral study with the new selective agonist AMN082

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Metabotropic glutamate receptors (mGluRs) have recently been shown to be implicated in neurodegenerative disorders, such as Parkinson’s disease (PD). Group III mGluRs are presynaptically located on glutamatergic and GABAergic neurons which are known to be overactive in animal models of PD; in consequence, the beneficial effects of drugs acting on group III mGluRs may be due to the reduction of both glutamatergic and GABAergic transmission. We reported previously that ACPT-1, a nonselective group III mGluRs agonist, injected locally into the globus pallidus, striatum or substantia nigra (SN), significantly attenuated the haloperidol-induced catalepsy in rats. Recently N,N’-dibenzhydryl-ethane-1,2-diamine dihydrochloride (AMN082), a new potent, subtype-selective and brain-penetrable mGluR7 agonist, has been synthesized. Within the basal ganglia, the density of mGluR7 is the highest in the striatum and SN. Therefore, the aim of the present study was to determine: (1) whether the selective activation of mGluR7 by systemic administration of AMN082 could produce antiparkinsonian-like effects in the haloperidol-induced catalepsy and reserpine-induced akinesia models in rats; (2) whether striatal mGluR7 could contribute to that effect. We found that AMN082 (1 and 3 mg/kg, ip) decreased the haloperidol (0.25 mg/kg, ip)-induced catalepsy, but was ineffective in attenuating the reserpine (2.5 mg/kg, ip)-induced akinesia. An anticonataleptic effect was also observed after bilateral administration of AMN082 (1.2 ng and 3.5 ng/0.5 μl) into the striatum. The above findings provide the first evidence that the activation of mGluR7 may produce antiparkinsonian-like effects in rats. Furthermore, our results demonstrate the contribution of striatal mGluR7 to the anticonataleptic effects of AMN082.