

BLOCKADE OF PALLIDAL ADENOSINE A_{2A} RECEPTORS POTENTIATES CONTRALATERAL ROTATIONAL BEHAVIOR INDUCED BY L-DOPA AND DOPAMINERGIC AGONISTS IN HEMIPARKINSONIAN RATS

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The globus pallidus (GP), one of the main projection areas of the striatum, is the principal component of the basal ganglia circuitry. There is growing evidence that the adenosine A_{2A} receptor serves to play a crucial role in basal ganglia function, particularly in the control of motor behaviour; furthermore adenosine A_{2A} antagonists have been shown to exhibit a prominent anti-Parkinsonian activity in several animal models. An involvement of GP in the antiparkinsonian effects of A_{2A} receptor antagonists has been proposed on the basis of the selective localization of A_{2A} receptors on the striatopallidal pathway. Evidence has shown that A_{2A} receptors are expressed in GP at medium-high level; moreover, both adenosine A_{2A} agonists and antagonists modulate the extracellular concentrations of GABA. Those studies suggest that, besides striatum, A_{2A} receptor antagonists might exert their antiparkinsonian activity at the level of GP. The aim of this study was to investigate the effect of the intrapallidal infusion of SCH BT2, a water-soluble analogue of the A_{2A} antagonist SCH 58261, on contralateral turning behavior, induced by dopamine receptor agonists, in the unilaterally 6-hydroxydopamine rat model of Parkinson's Disease. SCH BT2 (5µg/1µl) altered neither motor behavior nor produced postural asymmetry by itself. However, when infused simultaneously with a parenteral subthreshold dose of L-DOPA (3 mg/kg i.p.) which elicited scarce contralateral rotational behavior (34.7±20.7/1h), SCH BT2 significantly potentiated the number of contraversive rotations (167.4±16.3/1h). SCH BT2 significantly potentiated quinpirole (0.05 mg/kg s.c.) induced turning behavior (45.3±16.5/1h vs 7.5±1.9/1h) and SKF 38393 (1.5 mg/kg s.c.) induced contraversive rotations (812±109/3h vs 314.4±127/3h). These results indicate that blockade of pallidal A_{2A} receptors enhances the behavioral effects of dopamine receptor stimulation in 6-OHDA-lesioned rats, suggesting that GP may be involved in the antiparkinsonian effects of A_{2A} antagonists. Furthermore, the potentiation of D₁-mediated effects observed, suggests that the GP may be a central area in the basal ganglia circuit for modulation of both D₁ and D₂ mediated motor responses.