

SYNERGISTIC EFFECT OF SCH 58261, AN ADENOSINE A_{2A} RECEPTOR ANTAGONIST, AND L-DOPA ON THE RESERPINE-INDUCED MUSCLE RIGIDITY IN RATS

Jadwiga Wardas[#]

Department of Neurosychopharmacology, Institute of Pharmacology, Polish Academy of Sciences, Smętna 12, PL 31-343 Kraków, Poland

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The aim of the present study was to find out whether a blockade of adenosine A_{2A} receptors by the selective antagonist, SCH 58261, potentiates the attenuating effect of L-DOPA, the well-known antiparkinsonian drug, on parkinsonian-like muscle rigidity in rats. Muscle tone was examined using a combined mechano- and electromyographic method, which simultaneously measured muscle resistance of a rat hindfoot to passive extension and flexion in the ankle joint and the electromyographic (EMG) activity of the antagonistic muscles of that joint: gastrocnemius and tibialis anterior. Muscle rigidity was produced by reserpine (5 mg/kg *ip*) injected in combination with α -methyl-p-tyrosine (α -MT, 250 mg/kg *ip*). L-DOPA (25 mg/kg *ip*) or SCH 58261 (0.1 mg/kg *ip*) administered separately, slightly influenced the reserpine + α -MT-induced muscle rigidity. However, only ankle joint extension was affected significantly while the effect on flexion of the rat hindfoot was not significant. Neither L-DOPA nor SCH 58261 given separately modified the reserpine-enhanced tonic or reflex EMG activities in both muscles examined. However, when L-DOPA (25 mg/kg) was given together with SCH 58261 (0.1 mg/kg), a clear synergistic effect was seen on both examined movements and muscles. The present results show that the blockade of adenosine A_{2A} receptors potentiates the antiparkinsonian effect of L-DOPA. Since such an effect was seen in different animal models of Parkinson's disease (PD), it seems that co-administration of SCH 58261 may allow for the lowering of the doses of L-DOPA in clinical practice, which indicates a potential therapeutic value of this compound in the treatment of PD.

Key words: adenosine A_{2A} receptors, L-DOPA, mechano- and electromyogram, muscle rigidity, parkinsonism, reserpine, SCH 58261

[#] e-mail: wardas@if-pan.krakow.pl