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ALPHA2C-ADRENOCEPTOR ACTIVATION REDUCES DOPA UPTAKE IN HUMAN NEUROBLASTOMA SH-SY5Y CELLS

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Alpha2C-adrenoceptor antagonists have been proposed has having therapeutic value in the treatment of neuropsychiatric disorders such as schizophrenia and drug withdrawal. Mice with targeted deletion or selective pharmacological inhibition of alpha2C-adrenoceptors presented higher brain tissue levels of dopamine and its precursor 3,4-dihydroxyphenylalanine (DOPA). In this study we investigated the effect of alpha2C-adrenoceptor activation on DOPA uptake in a human neuroblastoma cell line (SH-SY5Y). DOPA levels in cells were evaluated by high performance liquid chromatography with electrochemical detection. Results are presented as arithmetic mean ± standard error. SH-SY5Y cells take up DOPA in a time dependent (linear until 6 minutes) and concentration dependent (2.5-2500μM) manner. Non-linear analysis of the saturation curves revealed for DOPA a Km (in μM) of 435±91 and a Vmax (in nmol/mg protein/6 min) of 465±30. The uptake of DOPA was inhibited by BCH and neutral amino acids but no by MeAIB and the acidic and basic aminoacids. DOPA uptake was unaltered by lowering the pH. In the absence of sodium there was a 20% reduction in the Vmax values for DOPA uptake. For a single concentration of DOPA, incubation with different concentrations of the alpha2-adrenoceptor agonist medetomidine (0.1-1000nM) produced a concentration dependent decrease in DOPA uptake (IC50 in nM: 8±0.3; Emax in % of inhibition: 55±5). Pre-incubation with the selective alpha2C-antagonist JP-1302 (300nM) abolished the reduction produced by incubation medetomidine. In conclusion, in SH-SY5Y cells DOPA uptake is promoted by the LAT (sodium independent) and B0 (sodium dependent) systems and is inhibited by activation of alpha2C-adrenoceptors.

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