Pharmacological Characterization of the NMDA Receptor in the Human Platelet

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Abstract

N-methyl-D-aspartate (NMDA) receptors have critical roles in excitatory synaptic transmission, plasticity and excitotoxicity in the CNS. These receptors also have been implicated in many physiological processes such as information processing; learning and memory, and in pathological processes such as hypoxia, degenerative diseases and drug-addicted brain damage. More recently, NMDA receptors were found in non-neuronal tissues such as bone, pancreas and skin. This study aimed to investigate NMDA receptor in human platelet. By using platelet aggregation study, the MK801 which is a non-competitive antagonist in the channel of NMDA receptor can inhibit platelet aggregation induced by ADP around 40-50%. By using radioligand binding study with centrifugation technique, [^{3}H] MK801 can bind to platelet with high affinity (Kd 27.99+/-6.12 nM, Bmax 888.76 +/-67.95 fmol/mg protein). The displacement of 0.5 nM [^{3}H] MK801 in platelet by channel blockers was monophasic (rank order: MK801> memantine> ketamine). In this study, binding properties of NMDA receptor of platelet were compared to rat brain (Kd 1.308+/-0.13 nM, Bmax 3075.33+/-112.86 fmol/mg protein) and rank order of channel blockers displacement were MK801> ketamine > memantine. This technique is applied to study the role of native human NMDA receptor as a marker of brain damage in drug-addicted patient.

Keywords: NMDA receptor, brain damage, human platelet, rat brain, glutamate, MK801, ketamine, memantine