Abstract

N-methyl-D-aspartate (NMDA) receptors are a class of ionotropic glutamate receptors, involved in excitatory synaptic transmission, synaptic plasticity and excitotoxicity. They form heterotetrameric complexes composed of GluN1, GluN2A-D and/or GluN3A-B subunits that are activated by glutamate and glycine. Previous reports showed that different subunits of NMDA receptors, especially the GluN2 subunits, confer different functional and pharmacological properties on the receptor complexes. However, the subunit-dependent differences in the regulation of intracellular processing and transport of NMDA receptor subtypes has not been clearly elucidated. The aim of this work was to clarify the mechanisms of regulation of the NMDA receptor transport. In our experiments we performed immunocytochemistry of receptors on heterologous COS-7 cells and cultured cerebellar granule cells (CGC), both expressing recombinant NMDA receptors. The results of my work show that the transport of NMDA receptors is regulated by presence of GluN2A and GluN2B subunits. Our results further showed that transport of the GluN1/GluN2C receptors is regulated by three specific areas of the GluN2C subunit: i) the A2 segment within the amino-terminal domain, ii.) the M3 domain, and iii.) the proximal part of the C-terminus containing the sequence of five amino acids, SLPSP. Our results help clarify the mechanisms regulating the function of NMDA receptors in the mammalian central nervous system and thus contribute to our understanding of the mechanisms involved in various neurological and psychiatric disorders associated with abnormal regulation of NMDA receptors, such as Alzheimer's and Parkinson's dementia, schizophrenia, Huntington's disease, epilepsy, depression, schizophrenia, ischemia or cocaine addiction.