Protein kinase CK2 in postsynaptic densities: Phosphorylation of PSD-95/SAP90 and NMDA receptor regulation

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Protein kinase CK2 (CK2) is highly expressed in rat forebrain where its function is not well understood. Subcellular distribution studies showed that the catalytic subunit of CK2 (CK2?) was enriched in postsynaptic densities (PSDs) by 68%. We studied the putative role of CK2 activity on N-methyl-d-aspartate receptor (NMDAR) function using isolated, patch-clamped PSDs in the presence of 2 mM extracellular Mg 2+. The usual activation by phosphorylation of the NMDARs in the presence of ATP was inhibited by the selective CK2 inhibitor 5,6-dichloro-1-?-ribofuranosyl benzimidazole (DRB). This inhibition was voltage-dependent, i.e., 100% at positive membrane potentials, while at negative potentials, inhibition was incomplete. Endogenous CK2 substrates were characterized by their ability to use GTP as a phosphoryl donor and susceptibility to inhibition by DRB. Immunoprecipitation assays and 2D gels indicated that PSD-95/SAP90, the NMDAR scaffolding protein, was a CK2 substrate, while the NR2A/