

P005 Differential interaction of PSD-95 and Chapsyn-110
with NR1/NR2A, NR1/NR2B and NR1/NR2C, NR1/NR2D
NMDA receptors

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PSD-95 has multiple effects on NMDA receptors. Association with NR1/NR2B regulates cell surface receptors via inhibition of internalization; with NR1/NR2B, it facilitates phosphorylation/dephosphorylation via src and fyn and PTP ξ tyrosine phosphatase; it controls NR2B calpain-mediated cleavage; PSD-95 inhibits NR1/NR2A and NR1/NR2B protein kinase C-mediated potentiation and it contributes to cell surface expression via controlling the export of NR1-3a subunits from the endoplasmic reticulum. Previously we reported that association of PSD-95 with NR1/NR2A and NR1/NR2B results in a selective enhanced expression of NR2A and NR2B subunits and altered molecular pharmacological properties which led us to propose that association with PSD-95 results in a decreased gating of NMDA channels. NR2D-containing receptors are thought to be extra-synaptic perhaps due to lack of association with PSD-95. To address whether NR2D and the homologous NR2C subunit do associate with PSD-95, HEK 293 cells were co-transfected with NR1/NR2C or NR1/NR2D \pm PSD-95 or \pm Chapsyn-110. Association was determined by immunoprecipitation and quantitative immunoblotting. The results show that in heterologous systems, PSD-95 does associate with NR1/NR2C and NR1/NR2D. In contrast to NR1/NR2A and NR1/NR2B receptors however, no enhancement of NR2 subunits was observed suggesting differential interactions of NMDA receptor subtypes with scaffolding proteins and thereby possible differences in downstream signalling mechanisms. Supported by the BBSRC (UK).