Abstract: Molecular events associated with mnemonic processes and neuronal plasticity are postulated to result in functional changes in synaptic structure. One possible site is the postsynaptic density, where activity-dependent changes modulate signal transduction cascades. In this presentation data will be presented detailing spatial–temporal changes for phosphodiesterase 4B (PDE4B) proteins and their substrate cAMP within three neuronal fractions during early and late long-term potentiation (LTP). The cAMP-dependent protein kinase A cascade—which can be regulated by distinct PDE4B activity—is required for mnemonic processes as well as mechanisms of neuronal plasticity, such as those during maintenance or late-LTP. Fluorescence in situ hybridization studies (FISH) identified no translocation of PDE4B3 from the soma after late-LTP induction indicating a subtle, local control of PDE4B activity. Protein changes were detected within the PSD-enriched fraction. From these results, we conclude that either the changes in PDE4B are due to modulation of pre-existing mRNA, or that the protein is specifically translocated to activated synaptic structures. Furthermore, we report late changes in cAMP levels in the somato-dendritic fraction and discuss this result with the increased PDE4B1/3 doublet in the PSD-enriched fraction.