

P010 Vip/pacap38 and NMDA facilitate dendrite formation by modifying the activities of the small Rho GTPases and phosphoinositide 3-kinase

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During their development neurons polarize and elaborate dendrites and axons. The family of small Rho GTPases influences neuronal morphogenesis by regulating the assembly and stability of the actin cytoskeleton. Rac and Cdc42 facilitate the outgrowth of dendrites and branches, whereas Rho and Rho kinase seem to attenuate it. Phosphoinositide 3-kinase (PI3K) facilitates dendrite and branch retraction and also stimulates dendrite and branch addition by inhibiting the Rho/Rho kinase pathway. PACAP, VIP and its receptors are present in the developing nervous system and function as endogenous neurotrophic factors. In the present study we investigated the function of glutamate receptors of the NMDA type (NMDAR) and VIP/PACAP38 on the dendritic morphology in dissociated hippocampal neurons. Rac was only activated by NMDA, whereas Cdc42 was activated by NMDA, VIP and PACAP38. None of the substances alone reduced the activity of RhoA, but the combination of NMDA and VIP/PACAP decreased the activity of RhoA. PI3K activity was increased by NMDAR stimulation. VIP/PACAP alone did not influence the PI3K activity but both neuropeptides abolished the NMDA-induced PI3K activation. Also the Rho kinase inhibitor Y-27632 reduced the NMDAR induced PI3K activation. Thus the Rho/Rho kinase pathway seems to influence the NMDAR-induced PI3K activation. These biochemical data corresponded with our morphological finding that NMDA in combination with VIP/PACAP38 or Rho-kinase inhibition facilitates the formation of the dendritic tree.