

Oral presentation

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Regulation of cGMP by phosphodiesterases (PDEs) in the central nervous system

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It is becoming well established that metabolic inactivation of the cyclic nucleotides cAMP and cGMP is intimately involved in the regulation of cyclic nucleotide-mediated signaling cascades. There are four families of PDEs that metabolize cGMP, PDE1, PDE2, PDE9, and PDE10, that are prominently and differentially expressed in the central nervous system. We have begun to characterize the role of these enzymes on cGMP metabolism in vivo using pharmacological and genetic approaches in mice. The effects of manipulating enzyme activity differ for each enzyme in different brain regions, corresponding to differential localization. However, the involvement of each enzyme also appears dependent on the level of activation of cGMP formation. These findings begin to define and differentiate the functions for the different PDEs in regulating cGMP signaling in the central nervous system.