The Antidepressant and Antiinflammatory Effects of Rolipram in the Central Nervous System

Jie Zhu, Eilhard Mix, Bengt Winblad

Division of Geriatric Medicine, Department of Clinical Neuroscience, Karolinska Institutet, Huddinge University Hospital, Stockholm, Sweden; Department of Neurology, University of Rostock, Rostock, Germany

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ABSTRACT

Rolipram is a selective inhibitor of phosphodiesterases (PDE) IV, especially of the subtype PDE IVB. These phosphodiesterases are responsible for hydrolysis of the cyclic nucleotides cAMP and cGMP, particularly in nerve and immune cells. Consequences of rolipram-induced elevation of intracellular cAMP are increased synthesis and release of norepinephrine, which enhance central noradrenergic transmission, and suppress expression of proinflammatory cytokines and other mediators of inflammation. In humans and animals rolipram produces thereby a variety of biological effects. These effects include attenuation of endogenous depression and inflammation in the central nervous system (CNS), both effects are of potential clinical relevance. There are some discrepancies between in vitro and in vivo effects of rolipram, as well as between results obtained in animal models and clinical studies. The clinical use of rolipram is limited because of its behavioral and other side effects. Newly developed selective PDE IV inhibitors with presumably higher potency and lower toxicity are currently under investigation.