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Intracellular free Ca²⁺ increases with advancing age in adult. Drugs that alter Ca²⁺ levels, either by blocking voltage-dependent (e.g. nimodipine) or enhancing NMDA receptor function (e.g. D-2-lysine), alter hippocampal neuronal excitation and improve the learning ability of aging subjects that are learning-impaired compared to younger controls. Changes in the expression of the voltage-sensitive L-type and N-type Ca²⁺ channels (including receptors and voltage-gated ion channels) are critically involved in neuronal plasticity. The current study focused on age-related changes in the expression of both L-type, CAM-KII, and N-type, calcineurin, that are part of the Ca²⁺-activated Ca²⁺ channel (via the potent calcium-binding protein, calmodulin, and have been implicated in regulating neuronal plasticity. If alterations in CAM-KII and calcineurin activity are required for the storage of new associations, and aging subjects are impaired in making new associations, then the expression or activity of these enzymes may be altered in the aging hippocampus and other brain regions crucially involved in learning and memory.

Standard immunohistochemical methods, using commercial (Sigma-RBI) rabbit polyclonal antibodies, were used to assess the expression of CAM-KII and calcineurin in the hippocampus and other brain regions in serial 10 µm paraffin sections of young (3-4 mo) and old (30 mo) male rats. All immunostaining was done in parallel to avoid artificial variance. The pattern of immunoreactivity for CAM-KII and calcineurin was comparable using immunocytochemistry. Calcineurin immunoreactivity was higher in hippocampal regions of young rats, with age-dependent changes observed. Basal CAM-KII immunoreactivity was lower than that for calcineurin, again with age-dependent changes in expression observed. Thus, it appears likely that changes in the expression of calcium-calmodulin-dependent kinases and phosphates may play a significant role in age-dependent deficits in learning and memory. Supported by Human Development funds.

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