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Activity:

Evaluation of aging-related changes in calcium binding proteins in rat medial prefrontal cortex

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Endogenous calcium binding proteins (CaBPs) are intracellular proteins that help in regulating calciumdependent processes. Certain CaBPs, like calbindin (CB), may also provide a valuable neuroprotective function by minimizing the ability of excess intracellular calcium to trigger cell death cascades. Thus, an aging-related loss of CaBPs may contribute to an increased vulnerability of certain populations of neurons to neurodegenerative disorders, including Alzheimer's disease and stroke. The medial prefrontal cortex (mPFC) is involved in a variety of behavioral tasks, particularly those that require modification of existing behaviors. Extinction of conditioned fear is one such task that we have recently shown to be impaired as a function of aging. In an attempt to determine whether changes in CaBPs may contribute to our observed aging-related extinction deficits, we have begun evaluating CaBPs in key brain regions (hippocampus and mPFC) known to be susceptible to neurodegenerative disorders. Furthermore, information gained from these studies will help us further evaluate the feasibility of targeting CaBPs in developing novel neurotherapeutics (e.g., we recently demonstrated that the CaBP aequorin is neuroprotective when administered to hippocampal neurons prior to ischemia). In the present studies, CB and calmodulin (CaM), were studied in hippocampus and mPFC from adult (3 mo.) and aged (23 mo.) rats using Western blot analysis. After dissecting out dorsal and ventral hippocampus as well as the infralimbic (IL) and prelimbic (PL) subdivisions of mPFC, tissues were homogenized, the samples were normalized for total protein, and then subjected to SDS-PAGE. The proteins were then transferred to PVDF membranes and then incubated with anti-CB and anti-CaM primary antibodies. HRP-conjugated secondary antibodies were used to visualize the proteins. After development, the immunoblots were then analyzed using Image J. Within each brain region, the aged bands were compared to their corresponding adult control bands. Preliminary results suggest a selective decrease in CB and CaM protein expression in IL (aged CB: 41% decrease; aged CaM: 63% decrease) but not PL. No obvious differences were observed in dorsal or ventral hippocampus. These region-specific changes in mPFC may contribute to our observed aging-related extinction deficits. Furthermore, the depletion of CaBPs in IL may leave this region more susceptible to excitotoxic cell death. These data suggest that targeting CaBPs may be a useful approach for developing novel therapeutics for protecting neurons against aging-related neurodegenerative disorders.

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