Name(s)	Project Number
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Project Title

Different Caspases Mediate Age-Related Apoptosis in Neurons Compared with Astrocytes

Abstract

Objectives/Goals

Apoptosis is a cell suicide program; however, effects of age and cell type on apoptosis in the brain are poorly understood. The age at which different brain cells are most susceptible to apoptosis is unclear.

Methods/Materials

Neuron and astrocyte cultures were deprived of serum. To characterize DNA fragmentation, Terminal deoxynucleotidyl transferase-mediated dUTP labeling (TUNEL) staining was performed. To identify apoptotic or necrotic cells in cultured cell population, Hoechst and Propidium Iodide (PI) staining were performed. Cell injury was quantified through lactate dehydrogenase (LDH) assay. Caspase and MAP kinase phosphorylation were measured using immuno-blotting. Caspase 3, 8 and 9 were also inhibited in both cultures to determine its role in determining age-related differences. All data were analyzed by one-way analysis of variance (ANOVA), followed by two-tailed Student's t-test.

Results

Young neurons showed more apoptosis and greater caspase (essential protease for apoptosis) expressions compared to mature neurons. Mature neurons and astrocytes were found to be less vulnerable to serum deprivation and to undergo necrosis rather than apoptosis, which correlates with a lack of caspase activity and TUNEL-positive cells. Astrocytes showed condensed but non-fragmented nuclei and a different caspase expression.

Conclusions/Discussion

Caspase 3, 8, and 9 contribute to neuronal apoptosis while caspase 11 seems important to astrocytes. Our findings suggest that neurons and astrocytes utilize different apoptotic pathways as they develop and anti-apoptotic interventions against brain injury should be developmentally targeted and specific to cell type

Summary Statement

Caspases differentiate neurons and astrocytes; they contribute to the different apoptotic pathways.

Help Received